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OM protein - protein search, using sw model

Run on: February 25, 2004, 16:12:26; Search time 60 Seconds

(without alignments)

1492.793 Million cell updates/sec

Title:

US-09-787-126-2

Perfect score: 1685

Sequence:

1 MRRASRDYTKYLRGSEEMGG.....LLDPDQDATYFGAFKVRDID 317

Scoring table: BLOSUM62

Gapop 10.0 , Gapext 0.5

Searched:

1586107 seqs, 282547505 residues

Total number of hits satisfying chosen parameters: 1586107

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%

Maximum Match 100%

Listing first 45 summaries

Database :

A_Geneseq 29Jan04:*

1: geneseqp1980s:*

2: geneseqp1990s:* 3: geneseqp2000s:*

4: geneseqp2001s:*

5: geneseqp2002s:*

6: geneseqp2003as:*

7: geneseqp2003bs:*

8: geneseqp2004s:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

			8							
Resi	ılt		Query							
N	10. 	Score	Match	Length	DB	ID		Descript	ion	
	1	1685	100.0	317	2	AAW83195			Human	ost
	2	1685	100.0	317	2	AAW69957		Aaw69957	NF-kB	rec
	3	1685	100.0	317	2	AAW68293		Aaw68293		
	4	1685	100.0	317	2	AAE08738		Aae08738	Human	rec
	5	1685	100.0	317	3	AAY84417		Aay84417		
	6	1685	100.0	317	4	AAE04426		Aae04426		
	7	1685	100.0	317	4	AAE01993		Aae01993		
	8	1685	100.0	317	5	ABB08134		Abb08134		
	9	1685	100.0	317	5	AAE26103		Aae26103		

10	1685	100.0	317	5	ABG31631		Human RAN
11	1685	100.0	317	5	AAU78285	Aau78285	Human TRA
12	1685	100.0	317	5	AA019096		C neoform
13	1685	100.0	317	6	ABP55108		Human ost
14	1685	100.0	317	6	AAE34364	Aae34364	Human rec
15	1685	100.0	317	6	ABR42314	Abr42314	Human RAN
16	1685	100.0	317	7	ADB16988	Adb16988	Human rec
17	1685	100.0	317	7	ADC35204	Adc35204	Human TNF
18	1685	100.0	317	7	ADC73002	Adc73002	Human RAN
19	1685	100.0	317	7	ADC78268	Adc78268	Human RAN
20	1677	99.5	317	2	AAW83018		Osteoclas
21	1417.5	84.1	316	2	AAW83017	Aaw83017	Osteoclas
22	1417.5	84.1	316	2	AAW83194	Aaw83194	Human ost
23	1417.5	84.1	316	2	AAW59654		Amino aci
24	1417.5	84.1	316	2	AAY17874		Murine TR
25	1417.5	84.1	316	3	AAY91024		Mouse OBM
26	1417.5	84.1	316	3	AAY84418		Amino aci
27	1417.5	84.1	316	3	AAY84419		Amino aci
28	1417.5	84.1	316	5	AAU78289		Mouse TRA
29	1417.5	84.1	316	6	ABR42071		Human RAN
30	1417.5	84.1	316	6	ABB99477		Amino aci
31	1417.5	84.1	316	6	ABU08463		Amino aci
32	1417.5	84.1	316	6	ABR55560		Amino aci
33	1396.5	82.9	318	4	AAB82092		Rat osteo
34	1326.5	78.7	294	2	AAW69956		NF-kB rec
35	1326.5	78.7	294	2	AAW68292		NF-kB rec
36	1326.5	78.7	294	2	AAE08737		Murine re
37	1326.5	78.7	294	4	AAE04425		Murine re
38	1326.5	78.7	294	4	AAE01992		Murine RA
39	1326.5	78.7	294	5	AAE26102	Aae26102	
40	1326.5	78.7	294	7	ADB16986	Adb16986	
41	1326.5	78.7	294	7	ADC73000		Murine RA
42	1326.5	78.7	294	7	ADC78266	Adc78266	
43	1325	78.6	250	6	ADA50079	Ada50079	
44	1322	78.5	250	6	ADA50095	Ada50095	
45	1322	78.5	250	6	ADA50094	Ada50094	
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ALIGNMENTS

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RESULT 1
AAW83195
    AAW83195 standard; protein; 317 AA.
ΙD
XX
AC
    AAW83195;
XX
DT
     11-FEB-1999 (first entry)
XX
    Human osteoprotegerin binding protein from the pcDNA/huOPGbp1.linsert.
DΕ
XX
     Human; osteoprotegerin binding protein; OPG binding protein; arthritis;
KW
     osteoporosis; osteoclast maturation; bone disease; metastasis; ODAR;
KW
KW
     hypercalcaemia; osteoclast differentiation and activation receptor;
KW
     Paget's disease.
XX
OS
     Homo sapiens.
```

```
XX
PN
     WO9846751-A1.
XX
PD
     22-OCT-1998.
XX
PF
     15-APR-1998;
                   98WO-US007584.
XX
PR
     16-APR-1997:
                   97US-00842842.
PR
     23-JUN-1997;
                   97US-00880855.
PR
     30-MAR-1998;
                   98US-00052521.
XX
PΑ
     (AMGE-) AMGEN INC.
XX
PΙ
     Boyle WJ;
XX
     WPI; 1998-594578/50.
DR
     N-PSDB; AAV70285.
DR
XX
     Nucleic acid encoding osteoprotegrin binding protein - useful for, e.g.
PT
PT
     treating bone diseases by modulating osteoclast differentiation and for
PT
     diagnosis.
XX
PS
     Claim 19; Fig 4; 47pp; English.
XX
     The present sequence is human osteoprotegerin (OPG) binding protein. Host
CC
     cells transfected with vectors containing nucleic acid molecules encoding
CC
     OPG binding protein are used to produce recombinant OPG binding protein.
CC
CC
     OPG binding protein is used in binding assays to determine osteoprotegrin
CC
     (OG) in biological samples; to screen for specific binding agents
     (particularly agonists and antagonists, including intracellular proteins)
CC
CC
     ; to raise Ab (useful in immunoassays for detection of OPG binding
CC
     protein) and to identify compounds that modulate binding of OPG binding
CC
     protein to osteoclast differentiation and activation receptor (ODAR). The
CC
     nucleic acid molecule encoding OPG binding protein can be used to detect
     OPG binding protein-encoding sequences, e.g. screening for related
CC
CC
     sequences, also to produce transgenic animal models, while complementary
CC
     sequences are used for antisense regulation of OPG binding protein
     expression. Modulators of OPG binding protein, particularly soluble forms
CC
CC
     of OPG binding protein or Ab, are used to treat or prevent bone diseases,
     e.g. osteoporosis, bone loss caused by arthritis or metastases,
CC
    hypercalcaemia, Paget's disease, periodontal disease, osteoporosis,
CC
CC
    loosening of prostheses, optionally in combination with agents that
CC
    promote bone growth
XX
SO
    Sequence 317 AA;
  Query Match
                         100.0%; Score 1685; DB 2; Length 317;
  Best Local Similarity
                        100.0%; Pred. No. 4.3e-154;
 Matches 317; Conservative
                              0; Mismatches
                                                0; Indels
                                                              0;
Qγ
           1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
             Db
           1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
Qу
          61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
             61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
Db
```

```
121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
 Qу
             Db
         121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
         181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
 Qу
             181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
 Db
         241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Qу
             241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Db
Qу
         301 PDQDATYFGAFKVRDID 317
             1111111111111111
Db
         301 PDQDATYFGAFKVRDID 317
RESULT 2
AAW69957
     AAW69957 standard; protein; 317 AA.
XX
АC
     AAW69957;
XX
DT
     08-OCT-1998 (first entry)
XX
DE
    NF-kB receptor activator RANK ligand (RANKL).
XX
KW
     RANK; necrosis factor-kappa B; NF-kB; receptor activator; human;
     immune response; inflammatory response; toxic shock; sepsis; RANKL;
KW
    RANK ligand; tumour necrosis factor; TNF.
KW
XX
OS
    Homo sapiens.
XX
    W09828426-A2.
ΡN
XX
PD
    02-JUL-1998.
XX
PF
    22-DEC-1997;
                 97WO-US023775.
XX
PR
    23-DEC-1996;
                  96US-0059978P.
PR
    07-MAR-1997;
                  97US-00813509.
PR
    14-OCT-1997;
                  97US-0064671P.
XX
    (IMMV ) IMMUNEX CORP.
PA
XX
PΙ
    Anderson DM, Galibert LJ, Maraskovsky E;
XX
    WPI; 1998-377657/32.
DR
DR
    N-PSDB; AAV41378.
XX
    New isolated ligand for receptor activator of NF-kappa B - used to
PΤ
    develop products for augmenting an immune response for inhibiting an
PT
PT
    inflammatory response and for protection of cells.
XX
PS
    Claim 27; Page 59-60; 80pp; English.
XX
```

```
This represents a human RANKL, a ligand for the RANK (receptor activator
 CC
     of necrosis factor-kappaB (NF-kB)) polypeptide. RANK is a member of the
 CC
     tumour necrosis factor (TNF) family. A soluble RANK may be used for
     inhibiting activation of NF-kB, by contacting a cell expressing membrane-
 CC
     associated RANK with a soluble RANK which binds to RANK ligand (RANKL).
CC
CC
     RANKL polypeptides can activate RANK and can be used to induce maturation
     of dendritic cells and enhance their allo-stimulatory capacity, thereby
CC
     augmenting an immune response. The soluble RANK polypeptide composition
CC
     may also be used for regulating an immune or inflammatory response.
CC
CC
     Inhibition of NF-kB by RANK antagonists may be useful in ameliorating
     negative effects of an inflammatory response that result from triggering
CC
     of RANK, e.g. in treating toxic shock or sepsis, graft-versus-host
CC
CC
     reactions, or acute inflammatory reactions. They can also be used in
     adjunct therapy for disease characterised by neoplastic cells that
CC
     express RANK. RANKL polypeptides can also be used to identify inhibitors
CC
     of RANK and thus inhibitors of an inflammatory response, and also for
CC
CC
     protecting RANK-expressing cells from the negative effects of
     chemotherapy or the presence of high levels of TNF-alpha. The products
CC
CC
     can also be used for detection and drug screening
XX
SQ
     Sequence 317 AA;
  Query Match
                       100.0%; Score 1685; DB 2; Length 317;
  Best Local Similarity
                       100.0%; Pred. No. 4.3e-154;
  Matches 317; Conservative 0; Mismatches
                                            0; Indels
                                                          0; Gaps
                                                                     0;
           1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
Qу
             1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
Db
          61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
Qу
             Db
          61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
Qу
         121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
             Db
         121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
Qу
         181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
             Db
         181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
         241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
QУ
            Db
         241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
         301 PDQDATYFGAFKVRDID 317
Qу
            Db
         301 PDQDATYFGAFKVRDID 317
RESULT 3
AAW68293
    AAW68293 standard; protein; 317 AA.
XX
AC
    AAW68293;
```

CC

```
DT
      08-OCT-1998 (first entry)
XX
DE
     NF-kB receptor activator RANK ligand (RANKL).
XX
KW
      RANK; necrosis factor-kappa B; NF-kB; receptor activator; human;
KW
      immune response; inflammatory response; toxic shock; sepsis; RANKL;
KW
     RANK ligand; tumour necrosis factor; TNF.
XX
OS
     Homo sapiens.
XX
PN
     WO9828424-A2.
XX
PD
     02-JUL-1998.
XX
PF
     22-DEC-1997;
                    97WO-US023866.
XX
PR
     23-DEC-1996;
                    96US-0059978P.
PR
     07-MAR-1997;
                    97US-00813509.
PR
     14-OCT-1997;
                    97US-0064671P.
XX
PA
     (IMMV ) IMMUNEX CORP.
XX
PΙ
     Anderson DM, Galibert LJ, Maraskovsky E;
XX
     WPI; 1998-377655/32.
DR
DR
     N-PSDB; AAV41372.
XX
PT
     New isolated receptor activator of necrosis factor-kappa B - useful for,
     e.g. developing products for regulating an immune or inflammatory
PT
PT
     response, treating toxic shock or sepsis.
XX
PS
     Example 7; Page 59-60; 80pp; English.
XX
CC
     This represents a human RANKL, a ligand for the RANK (receptor activator
     of necrosis factor-kappaB (NF-kB)) polypeptide. RANK is a member of the
CC
CC
     tumour necrosis factor (TNF) family. Host cells transformed or
CC
     transfected with an expression vector comprising the RANK encoding
CC
     nucleic acid can be used to produce recombinant RANK protein. The soluble
CC
     RANK may be used for inhibiting activation of NF-kB, by contacting a cell
     expressing membrane-associated RANK with a soluble RANK which binds to
CC
     RANK ligand (RANKL). The soluble RANK polypeptide composition may also be
CC
CC
     used for regulating an immune or inflammatory response. Inhibition of NF-
CC
     kB by RANK antagonists may be useful in ameliorating negative effects of
CC
     an inflammatory response that result from triggering of RANK, e.g. in
CC
     treating toxic shock or sepsis, graft-versus-host reactions, or acute
CC
     inflammatory reactions. They can also be used in adjunct therapy for
CC
     disease characterised by neoplastic cells that express RANK. The products
CC
     can also be used for detection and drug screening
XX
SO
     Sequence 317 AA;
  Query Match
                         100.0%; Score 1685; DB 2; Length 317;
 Best Local Similarity
                         100.0%; Pred. No. 4.3e-154;
 Matches 317; Conservative
                               0; Mismatches
                                                  0;
                                                     Indels
                                                                0; Gaps
                                                                            0;
           1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
QУ
```

```
Db
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Qу
             Db
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Qу
             Db
         121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
         181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
Qy
             181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
Db
         241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Qу
             Db
         241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Qу
         301 PDQDATYFGAFKVRDID 317
             Db
         301 PDQDATYFGAFKVRDID 317
RESULT 4
AAE08738
ID
    AAE08738 standard; protein; 317 AA.
XX
AC
    AAE08738;
XX
    15-NOV-2001 (first entry)
DT
XX
DΕ
    Human receptor activator of NF kappaB ligand (RANKL) protein.
XX
KW
    Human; receptor activator of nuclear factor kappaB ligand; RANKL; NF;
KW
    tumour necrosis factor; TNF; TNF receptor associated factor; TRAF;
KW
    immune response; inflammatory response; graft-versus-host reaction;
    toxic shock; sepsis; acute inflammatory reaction; bone resorption;
KW
KW
    anti-apoptotic signal; therapy; immunosuppressant; anti-inflammatory.
XX
OS
    Homo sapiens.
XX
PN
    US6271349-B1.
XX
PD
    07-AUG-2001.
XX
PF
    17-DEC-1998;
                 98US-00215649.
XX
PR
    23-DEC-1996:
                 96US-0059978P.
PR
    23-DEC-1996;
                 96US-00772330.
PR
    07-MAR-1997;
                 97US-0077181P.
PR
    07-MAR-1997;
                 97US-00813509.
PR
    14-OCT-1997;
                 97US-0064671P.
PR
    22-DEC-1997;
                 97US-00996139.
XX
PΑ
    (IMMV) IMMUNEX CORP.
XX
PΙ
    Dougall WC, Galibert L;
```

```
XX
DR
     WPI; 1998-377655/32.
DR
     N-PSDB; AAD15311.
XX
     New isolated receptor activator of necrosis factor-kappa B - useful for,
PT
PT
     e.g. developing products for regulating an immune or inflammatory
PT
     response, treating toxic shock or sepsis.
XX
PS
     Example 15; Col 71-72; 47pp; English.
XX
CC
     The patent discloses novel receptor activator of nuclear factor (NF)-
     kappaB (RANK) proteins and their corresponding DNAs. RANK is a member of
CC
     the tumour necrosis factor (TNF) receptor superfamily and associates with
CC
     TNF receptor associated factor (TRAF) 2 and 3 which are important in the
CC
     regulation of immune and inflammatory response. The receptors are useful
CC
CC
     for regulating immune response and in screening for inhibitors of these
CC
     receptors. The cytoplasmic domain of RANK is used in developing assays
CC
     for inhibitors of signal transduction, e.g. for screening the molecules
     that inhibit interaction of RANK with TRAF1, TRAF2, TRAF3, TRAF5 and
CC
     particularly TRAF6. NF-kappaB inhibition by RANK antagonists are useful
CC
CC
     in ameliorating the negative effects of an inflammatory response that
     result from triggering of RANK, e.g. in treating toxic shock or sepsis,
CC
CC
     graft-versus-host reactions, acute inflammatory reactions and the effects
CC
     of bone resorption. RANK acts as an anti- apoptotic signal and rescue the
     cells that express RANK from apoptosis. Soluble forms of the receptor are
CC
     used in vivo or in vitro based screening tests for agonists or
CC
CC
     antagonists of RANK activity, as antagonists of RANK-mediated NF-kappa B
CC
     activation, or to inhibit transduction of a signal via RANK. RANK
CC
     compositions are used in the development of both agonistic and
     antagonistic antibodies, or as an adjunct therapy for disease
CC
     characterised by neoplastic cells that express RANK. Compounds that
CC
CC
     interfere with RANK/TRAF6 interactions are useful for modulating the
     formation of osteoclasts from osteoclast precursors and for modulating
CC
CC
     osteoclast function and activities. They are used as inhibitors of
CC
    diseases associated with excess bone resorption and as immunosuppressants
CC
    or anti-inflammatory agents. The RANK DNAs are useful for the expression
CC
    of recombinant proteins, as probes for analysis of the presence or
CC
    distribution of RANK transcripts, while the proteins are useful in
CC
    preparing kits for the detection of soluble RANK, or monitor RANK-related
    activity. The present sequence is RANK ligand (RANKL) protein from human
CC
XX
SO
    Sequence 317 AA;
 Query Match
                         100.0%; Score 1685; DB 2; Length 317;
 Best Local Similarity
                         100.0%; Pred. No. 4.3e-154;
 Matches 317; Conservative
                              0; Mismatches
                                                0; Indels
                                                              0; Gaps
                                                                          0;
QУ
           1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
             Db
           1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
Qу
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61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120

121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180

Db

Qу

```
Db
          121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
 Qу
          181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
              Db
          181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
          241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Qу
              Db
          241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Qу
          301 PDQDATYFGAFKVRDID 317
              1111111111111
Db
          301 PDQDATYFGAFKVRDID 317
RESULT 5
AAY84417
     AAY84417 standard; protein; 317 AA.
ID
XX
AC
     AAY84417;
XX
     25-JUL-2000 (first entry)
DT
XX
DΕ
     Amino acid sequence of a human osteoprotegerin ligand (OPGL).
XX
KW
     Osteoprotegerin ligand; OPGL; osteoprotegerin; osteoclastogenesis;
KW
     tumour necrosis factor receptor; type II transmembrane protein;
     osteoclast differentiation; CSF-1; osteoclast activator; immune response;
KW
     osteoporosis; bone resorption.
KW
XX
OS
     Homo sapiens.
XX
FΗ
     Key
                    Location/Qualifiers
FT
     Region
                    49. .69
FT
                    /note= "transmembrane region"
FT
     Domain
                    70. .157
FT
                    /note= "extracellular stalk domain"
FT
     Region
                    158. .317
FT
                    /note= "active ligand moiety"
XX
     W0200015807-A1.
ΡN
XX
PD
     23-MAR-2000.
XX
    13-SEP-1999;
ΡF
                   99WO-DK000481.
XX
PR
     15-SEP-1998;
                  98DK-00001164.
    02-OCT-1998;
PR
                  98US-0102896P.
XX
PΑ
     (MEBI-) M & E BIOTECH AS.
XX
PΙ
    Halkier T, Haaning J;
XX
DR
    WPI; 2000-271444/23.
DR
    N-PSDB; AAZ99964.
XX
PT
    In vivo down-regulation of osteoprotegerin ligand (OPGL) activity used to
```

```
treat, prevent and ameliorate osteoporosis.
 XX
 PS
     Claim 19; Page 78-79; 110pp; English.
XX
     The present sequence represents a human osteoprotegerin ligand (OPGL).
 CC
     Osteoprotegerin is a secreted member of the tumour necrosis factor
 CC
CC
     receptor family, which blocks osteoclastogenesis in a dose dependent
     manner. The OPGL protein is synthesised as a type II transmembrane
CC
     protein. The murine and human OPGL polypeptides are 87% homologous. OPGL
CC
CC
     is a potent osteoclast differentiation factor when combined with CSF-1.
CC
     It is not capable of inducing osteoclast differentiation in the absence
     of CSF-1. OPGL is also an activator of mature osteoclasts. The
CC
     specification describes a method for the in vivo down-regulation of OPGL
CC
     activity in an animal. The method comprises using at least one OPGL
CC
     polypeptide or subsequence, and/or at least one OPGL analogue to induce
CC
CC
     an immune response in the animal. The method and OPGL polypeptide are
     useful for treating, preventing and ameliorating osteoporosis or other
CC
     diseases or conditions characterised by excessive bone resorption
CC
XX
SQ
     Sequence 317 AA;
  Query Match
                       100.0%; Score 1685; DB 3; Length 317;
  Best Local Similarity 100.0%; Pred. No. 4.3e-154;
  Matches 317; Conservative
                             0; Mismatches
                                             0; Indels
                                                         0;
                                                             Gaps
                                                                    0;
          1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
Qy
             Db
          1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
          61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
Qy
            61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
Db
         121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
Qу
            121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
Db
        181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
Qy
            181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
Db
        241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Qу
            241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Db
        301 PDQDATYFGAFKVRDID 317
Qу
            111111111
Db
        301 PDQDATYFGAFKVRDID 317
RESULT 6
AAE04426
    AAE04426 standard; protein; 317 AA.
XX
АC
    AAE04426;
XX
DT
    04-SEP-2001 (first entry)
```

PT

```
DE
      Human receptor activator of NF-chi B ligand (huRANKL) protein.
 XX
      Human; receptor activator of NF-chi B; RANK; tumour necrosis factor; TNF;
 KW
      CD40; TNF receptor-associated factor; TRAF; ligand; immune response;
 KW
 KW
      chromosome 18q22.1; huRANKL; chromosome 13q14; transmembrane protein.
 XX
 OS
     Homo sapiens.
 XX
 FH
     Key
                     Location/Qualifiers
 FT
     Region
                     162. .317
 FT
                     /note= "Receptor binding region"
XX
ΡN
     US6242213-B1.
XX
PD
     05-JUN-2001.
XX
PF
     22-DEC-1997;
                   97US-00995659.
XX
PR
     23-DEC-1996;
                   96US-0059978P.
PR
     23-DEC-1996;
                   96US-00772330.
PR
                    97US-0077181P.
     07-MAR-1997;
PR
     14-OCT-1997;
                    97US-0064671P.
XX
PΑ
     (IMMV) IMMUNEX CORP.
XX
PΙ
     Anderson DM;
XX
DR
     WPI; 2001-407216/43.
DR
     N-PSDB; AAD08715.
XX
     New DNA molecules, useful for producing ligands (which are useful for
PT
     regulating immune response and in screening for inhibitors of NF-chi B
PT
     receptor activator) of the receptor activator of NF-chi B (RANK).
PT
XX
PS
     Claim 1; Col 65-66; 43pp; English.
XX
     The present invention relates to receptor activator of NF-chi B (RANK)
CC
CC
     DNA. RANK is mapped to chromosome 18q22.1 and its ligand (RANKL) to
     chromosome 13q14. RANK and RANKL are type 1 and type 2 transmembrane
CC
     proteins respectively. RANK is a member of the tumour necrosis factor
CC
     (TNF) superfamily and it closely resembles CD40 in the extracellular
CC
     region. RANK associates with TNF receptor-associated factor (TRAF) 2 and
CC
    TRAF3. The DNA molecules are useful for producing ligands of RANK. The
CC
    ligands are useful for regulating immune response and in screening for
CC
    inhibitors of RANK. The present sequence is human RANKL (huRANKL) protein
CC
XX
SQ
     Sequence 317 AA;
 Query Match
                         100.0%; Score 1685; DB 4; Length 317;
 Best Local Similarity 100.0%; Pred. No. 4.3e-154;
 Matches 317; Conservative
                             0; Mismatches
                                                 0; Indels
                                                               0;
Qу
           1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
             Db
           1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
```

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Qу
          61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
             Db
          61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
         121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
Qу
             121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
Db
         181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
Qу
             Db
         181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
         241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Qy
             Ďb
         241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
QУ
         301 PDQDATYFGAFKVRDID 317
             111111111111111
Db
         301 PDQDATYFGAFKVRDID 317
RESULT 7
AAE01993
    AAE01993 standard; protein; 317 AA.
ΙD
XX
AC
    AAE01993;
XX
DT
    31-JUL-2001 (first entry)
XX
DE
    Human full-length RANKL (receptor activator of NF-kappaB ligand).
XX
    Human; receptor activator of NF-kappaB; RANK; nuclear factor-kappaB;
KW
KW
    NF-kappaB; tumour necrosis factor; TNF; type I transmembrane protein;
KW
    TNF receptor-associated factor; TRAF; RANK ligand; RANKL; osteopathic;
KW
    inflammatory reaction; bone resorption; gene therapy; immunomodulator;
    immune system dysfunction; familial expansile osteolysis; FEO;
KW
    early onset Paget's disease of bone; EP; cytostatic; chromosome 13q14.
KW
XX
OS
    Homo sapiens.
XX
ΡN
    WO200136637-A1.
XX
    25-MAY-2001.
PD
XX
    14-NOV-2000; 2000WO-US031459.
PF
XX
PR
    17-NOV-1999;
                 99US-00442029.
XX
PΑ
    (IMMV) IMMUNEX CORP.
XX
PΙ
    Anderson DM, Hughes AE;
XX
DR
    WPI; 2001-329222/34.
DR
    N-PSDB; AAD05904.
XX
PΤ
    New DNA encoding a receptor activator of NF-kappaB polypeptide for the
PT
    treatment of Pagets disease and Familial Expansile Osteolysis (FEO).
```

```
XX
 PS
     Disclosure; Page 76-77; 96pp; English.
XX
CC
     The present invention relates to a novel receptor, referred to as RANK
CC
     (receptor activator of NF (nuclear factor)-kappaB), a member of TNF
     (tumour necrosis factor) receptor superfamily. RANK is a Type I
CC
CC
     transmembrane protein that interacts with TNF receptor-associated factors
CC
     (TRAFs). Triggering of RANK by overexpression or co-expression of RANK
     and membrane bound RANK ligand (RANKL) results in upregulation of the
CC
CC
     transcription factor NF-kappaB, a ubiquitous transcription factor that is
     most extensively utilised in cells of the immune system. Inhibition of Nf
CC
     -kappaB by RANK antagonists is useful in ameliorating negative effects of
CC
     inflammatory reactions, and the effects of excess bone resorption. The
CC
     RANK DNAs, proteins and their analogues are useful for the preparation of
CC
     pharmaceutical compositions, for infecting target cells for use in gene
CC
     therapy applications in diagnosing diseases associated with RANK, and as
CC
CC
     targets for use in screening assays. They may be used in the treatment or
CC
     diagnosis of immune system dysfunction. The present invention also
CC
    encompasses gene therapy methods to correct gene-activating mutations,
    associated with e.g. familial expansile osteolysis (FEO) and early onset
CC
CC
    Paget's disease of bone (EP). The present amino acid sequence is full-
    length human RANKL (huRANKL) protein. The RANKL gene is located in
CC
CC
    chromosome 13q14
XX
SO
    Sequence 317 AA;
  Query Match
                       100.0%; Score 1685; DB 4; Length 317;
  Best Local Similarity
                       100.0%; Pred. No. 4.3e-154;
  Matches 317; Conservative
                           0; Mismatches
                                            0; Indels
                                                          0;
                                                              Gaps
                                                                     0:
           1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
Qу
             1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
Db
          61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
Qу
            61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
Db
         121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
Qу
             Db
        121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
        181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
Qу
            181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
Db
        241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Qу
            241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Db
        301 PDQDATYFGAFKVRDID 317
Qу
            111111111111111
        301 PDQDATYFGAFKVRDID 317
Db
```

```
ID
      ABB08134 standard; protein; 317 AA.
 XX
 AC
      ABB08134;
 XX
 DT
      10-SEP-2002 (first entry)
 XX
 DE
      Human RANKL polypeptide.
 XX
 ΚW
      Dendritic cell; mobilisation factor; T cell; adjuvant; antibacterial;
 KW
      fungicide; protozoacide; virucide; anti-inflammatory; anti-HIV;
 KW
      tuberculostatic; cytostatic; human; RANKL.
 XX
 OS
      Homo sapiens.
 XX
 PN
      W0200236141-A2.
XX
 PD
      10-MAY-2002.
XX
PF
      30-OCT-2001; 2001WO-US044834.
XX
      02-NOV-2000; 2000US-0245721P.
PR
XX
PA
      (IMMV ) IMMUNEX CORP.
XX
     Lynch DH, De Smedt TN, Maliszewski CR, Butz EA, Miller RE;
PΙ
PΙ
     Thomas EK:
XX
DR
     WPI; 2002-500114/53.
XX
PT
     Treating an individual suffering from infection, e.g. inflammation,
     chickenpox or AIDS, by administering a combination of dendritic cell
PT
PΤ
     mobilization factor or maturation agent, T cell enhancing factor and
PT
     antigen-specific T cells.
XX
PS
     Disclosure; Page 42-43; 43pp; English.
XX
     The invention relates to treating an individual at risk for or suffering
CC
     from infection with a pathogenic or opportunistic organism. The method
CC
     involves administering a combination of two to five agents comprising:
CC
     (a) dendritic cell mobilisation factor; (b) dendritic cell maturation
CC
     agent; (c) dendritic cell activation agent; (d) T cell enhancing factor;
CC
     or (e) activated, antigen-specific T cells. The methods are useful for
CC
     treating an individual at risk for or suffering from infection with a
CC
     pathogenic or opportunistic organism, e.g. viruses (e.g. HIV), bacteria
CC
     (e.g. M. tuberculosis), yeast, fungi (e.g. C. albicans) or protozoa (e.g.
CC
CC
     T. cruzi, which causes Chaga's disease). The methods are especially
     useful for treating an individual suffering from immunosuppression by
CC
CC
     enhancing a lymphocyte-mediated immune response. In particular, the
    method is useful for treating inflammations, chickenpox, oral or genital
CC
    herpes, mononucleosis, multifocal leukoencephalopathy, hepatitis, AIDS, T
CC
    cell leukemia or T cell lymphoma. The activated antigen-presenting
CC
CC
    dendritic cells are useful as a vaccine adjuvant. The present sequence
CC
     represents a human RANKL polypeptide fragment
XX
SQ
     Sequence 317 AA;
```

```
Best Local Similarity 100.0%; Pred. No. 4.3e-154;
  Matches 317; Conservative
                            0; Mismatches 0; Indels
                                                            Gaps
                                                                   0;
Qу
           1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
             Db
           1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
QУ
          61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
             61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
Db
         121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
Qу
            121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
Db
         181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
QУ
            181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
Db
         241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Qу
            241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Db
Qу
         301 PDODATYFGAFKVRDID 317
            1111111111111111
Db
         301 PDQDATYFGAFKVRDID 317
RESULT 9
AAE26103
ID
    AAE26103 standard; protein; 317 AA.
XX
AC
    AAE26103;
XX
DT
    14-NOV-2002 (first entry)
XX
    Human RANK ligand (RANKL) protein.
DΕ
XX
    Human; RANK; receptor activator of nuclear factor-kappaB; NF-kB; sepsis;
KW
    immune response; toxic shock; graft-versus-host reaction; therapy; TRAF;
KW
    tumour necrosis factor receptor-associated factor; immunosuppressive;
KW
KW
    antibacterial; antiinflammatory; chromosome 13.
XX
OS
    Homo sapiens.
XX
ΡN
    US2002086827-A1.
XX
PD
    04-JUL-2002.
XX
PF
    30-MAY-2001; 2001US-00871291.
XX
PR
    23-DEC-1996;
                 96US-0059978P.
PR
    07-MAR-1997;
                97US-0077181P.
PR
    14-OCT-1997;
                97US-0064671P.
PR
    22-DEC-1997;
                97US-00996139.
PR
    17-DEC-1999;
                99US-00466496.
    24-MAY-2000; 2000US-00577800.
PR
```

```
PΑ
     (IMMV) IMMUNEX CORP.
 XX
 PΙ
     Anderson DM;
XX
DR
     WPI; 2002-642254/69.
     N-PSDB; AAD43213.
DR
XX
     A novel RANK (receptor activator of nuclear factor-kappaB (NF-kB))
PΤ
     polypeptide, useful for inhibiting activation of NF-kB and for regulating
PT
PT
     an immune or inflammatory response in an individual.
XX
     Example 15; Page 35; 49pp; English.
PS
XX
     The invention relates to novel RANK (receptor activator of nuclear factor
CC
CC
     -kappaB (NF-kB)) proteins and polynucleotides encoding them. Sequences of
     the invention are useful for inhibiting activation of NF-kappaB. They are
CC
     useful for regulating an immune or inflammatory response in an individual
CC
     at risk for an immune or inflammatory response. Inhibition of NF-kappaB
CC
    by RANK antagonists is useful in ameliorating negative effects of an
CC
     inflammatory response that results from triggering of RANK, for e.g. in
CC
CC
     treating toxic shock or sepsis, graft-versus-host reactions or acute
CC
    inflammatory reactions. Soluble RANK is useful as an adjunct therapy for
    diseases characterised by neoplastic cells that express RANK. Soluble
CC
    forms of the receptor are useful in vitro to screen for agonists or
CC
    antagonists of RANK activity. The cytoplasmic domain of RANK is useful in
CC
CC
    developing assays for inhibitors of signal transduction, to screen for
    molecules that inhibit interaction of RANK with tumour necrosis factor
CC
    receptor-associated factor (TRAF) 2 or TRAF3. The present sequence is
CC
    human RANK ligand (RANKL) protein. RANKL gene is located on chromosome 13
CC
XX
SO
    Sequence 317 AA;
  Query Match
                       100.0%; Score 1685; DB 5; Length 317;
  Best Local Similarity
                       100.0%; Pred. No. 4.3e-154;
  Matches 317; Conservative
                            0; Mismatches
                                             0; Indels
                                                          0;
                                                                     0;
Qу
          1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
            Db
          1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
          61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
Qу
            Db
         61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
        121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
QУ
            Db
        121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
        181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
QУ
            Db
        181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
        241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Qу
            241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Db
```

```
Qу
           301 PDQDATYFGAFKVRDID 317
               11111111111111
 Db
           301 PDQDATYFGAFKVRDID 317
 RESULT 10
 ABG31631
      ABG31631 standard; protein; 317 AA.
 ID
 XX
 AC
      ABG31631;
 XX
      29-NOV-2002 (first entry)
 DT
XX
DΕ
     Human RANKL protein.
XX
     Tumour; cancer; dendritic cell mobilisation factor; tumour-killing agent;
KW
KW
     dendritic cell maturation agent; T cell enhancing factor; skin cancer;
     antigen-specific T cell; prostate cancer; liver cancer; bone tumour;
KW
     brain tumour; spinal cord tumour; cervical intraepithelial neoplasia;
KW
     actinic keratosis; dendritic cell maturation stimulator; cytostatic;
KW
     dendritic cell activator; T cell enhancer; human; RANKL.
KW
XX
OS
     Homo sapiens.
XX
PN
     WO200266044-A2.
XX
PD
     29-AUG-2002.
XX
PF
     23-OCT-2001; 2001WO-US046254.
XX
     24-OCT-2000; 2000US-0242868P.
PR
XX
PΑ
     (IMMV ) IMMUNEX CORP.
XX
     Thomas EK, Lyman SD, Lynch DH, De Smedt TN, Maliszewski CR;
PΙ
XX
DR
     WPI; 2002-674891/72.
XX
     Treating an individual with tumors or cancers, e.g. liver cancer or brain
PT
     tumor, by administering a combination of dendritic cell populations, T
PT
PT
     cell enhancing factors and activated, antigen-specific T cells.
XX
PS
     Disclosure; Page 43-44; 44pp; English.
XX
     The present invention relates to a new method for treating a tumour-
CC
    bearing subject. The method involves administering a combination of 2 to
CC
     5 agents comprising dendritic cell mobilisation factor, dendritic cell
CC
    maturation agent, tumour-killing agent, T cell enhancing factor or
CC
    activated, antigen-specific T cells. The method is useful for treating
CC
    tumours or cancers in a subject e.g. skin cancer, prostate cancer, liver
CC
    cancer, tumours of the bone, brain or spinal cord, actinic keratosis, or
CC
    cervical intraepithelial neoplasia. The present amino acid sequence
    represents the human RANKL protein that was used in the method of the
CC
```

SQ Sequence 317 AA;

invention

CC

```
Query Match
                       100.0%; Score 1685; DB 5; Length 317;
  Best Local Similarity
                       100.0%; Pred. No. 4.3e-154;
  Matches 317; Conservative
                             0; Mismatches
                                             0; Indels
                                                         0;
                                                             Gaps
                                                                    0;
           1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
 Qу
             1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
 Db
          61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
Qу
             61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
Db
         121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
Qу
             121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
Db
Qу
         181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
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Qу
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Db
Qу
         301 PDQDATYFGAFKVRDID 317
            1111111111
Db
         301 PDQDATYFGAFKVRDID 317
RESULT 11
    AAU78285 standard; protein; 317 AA.
XX
AC
    AAU78285:
XX
DT
    18-JUN-2002 (first entry)
XX
DE
    Human TRANCE protein splice variant 1.
XX
    Human; tumour necrosis factor-related activation induced cytokine;
KW
    TRANCE; dwarfism; osteopetrosis; craniofacial-skeletal discrepancy;
KW
    bone damage; cartilage damage; traumatic injury; surgery; osteoarthritis;
KW
    rheumatoid arthritis; acromegaly; gigantism; exostosis; carilaginea;
KW
    exostosis bursata; multiple osteocartilaginous exostosis; chondrocyte;
KW
    cartilage growth; skeletal growth.
KW
XX
OS
    Homo sapiens.
XX
FH
    Key
                  Location/Qualifiers
FT
    Region
                  126. .317
                  /note= "Specifically claimed in claims 17 and 18"
FT
FT
    Region
                  137. .317
FT
                  /note= "Specifically claimed in claims 17 and 18"
FT
    Region
                  140. .317
                  /note= "Specifically claimed in claims 17 and 18" \,
FT
FΤ
    Region
                  145. .317
FT
                  /note= "Specifically claimed in claims 17 and 18"
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FT
      Region
                      158. .317
 FT
                      /note= "Specifically claimed in claims 17 and 18"
 FT
      Domain
                      159. .317
 FT
                      /note= "TNF core domain, specifically claimed in claims
 FT
                      17 and 18"
 XX
 PN
      W0200216551-A2.
 XX
 PD
      28-FEB-2002.
XX
     20-AUG-2001; 2001WO-US026101.
 PF
XX
PR
     18-AUG-2000; 2000US-0226197P.
XX
PΑ
     (UYMA-) UNIV MASSACHUSETTS MEDICAL CENT.
XX
PΙ
     Choi Y, Odgren PR, Marks SC;
XX
DR
     WPI; 2002-304119/34.
DR
     N-PSDB; ABK12876.
XX
PΤ
     Treating mammal having disorder characterized by abnormal
     cartilage/skeletal growth such as dwarfism, acromegaly, by administering
PT
     tumor necrosis factor-related activation induced cytokine-modulating
PT
PT
     agent to mammal.
XX
PS
     Disclosure; Fig 10; 55pp; English.
XX
     The present invention relates to a new method of treating a mammal having
CC
     a disorder comprising insufficient or excessive cartilage or skeletal
CC
CC
     growth. The method of the invention involves administering to the mammal
CC
     a tumour necrosis factor-related activation induced cytokine (TRANCE)-
     modulating agent. The method is useful for treating a mammal having a
CC
CC
     disorder comprising insufficient or excessive cartilage or skeletal
CC
     growth, where the disorder comprising insufficient cartilage or skeletal
     growth is selected from dwarfism, osteopetrosis, craniofacial-skeletal
CC
     discrepancies and bone or cartilage damage resulting from traumatic
CC
CC
     injury, surgery, osteoarthritis or rheumatoid arthritis, and disorders
     comprising excessive cartilage or skeletal growth are selected from
CC
     acromegaly, gigantism, exostosis, carilaginea, exostosis bursata and
CC
CC
     multiple osteocartilaginous exostoses. The method is useful for
CC
     inhibiting chondrocyte differentiation. The present amino acid sequence
     represents the human TRANCE protein, splice variant 1, of the invention.
CC
     TRANCE is a member of the tumour necrosis factor family and acts directly
CC
CC
     on cartilage-producing cells (chondrocytes)
XX
SQ
     Sequence 317 AA;
  Query Match
                          100.0%; Score 1685; DB 5; Length 317;
  Best Local Similarity
                         100.0%; Pred. No. 4.3e-154;
  Matches 317; Conservative
                               0; Mismatches 0; Indels
                                                                0; Gaps
                                                                             0;
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Qу
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Db
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 Db
         181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
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Db
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Db
Qу
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Db
         301 PDQDATYFGAFKVRDID 317
RESULT 12
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ID
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XX
AC
    AAO19096:
XX
    22-NOV-2002 (first entry)
DT
XX
    C neoformans antigen expressing dendritic cell related protein #5.
DE
XX
KW
    Human; fungicide; fungal infection; dendritic cell; antigen;
KW
    Cryptococcus neoformans; vaccine; immunostimulant.
XX
OS
    Homo sapiens.
XX
ΡN
    W0200266053-A2.
XX
PD
    29-AUG-2002.
XX
PF
    14-DEC-2001; 2001WO-US048288.
XX
PR
    04-JAN-2001; 2001US-0259653P.
XX
PA
    (IMMV) IMMUNEX CORP.
XX
PΙ
    Thomas EK:
XX
DR
    WPI; 2002-674896/72.
XX
PT
    Producing a population of activated, Cryptococcus neoformans antigen-
    presenting dendritic cells for preventing or treating C. neoformans
PT
    infection comprises causing the obtained dendritic cells to present the
PT
PT
    antigen.
XX
PS
    Disclosure; Page 30-32; 32pp; English.
XX
    The present invention relates to a method of producing a population of
CC
```

```
activated, Cryptococcus neoformans antigen-presenting dendritic cells,
     comprising causing the obtained dendritic cells to present the antigen
 CÇ
     and maturing the dendritic cells. The activated, C. neoformans antigen-
 CC
     expressing dendritic cells are useful for treating, or as vaccines or
 CC
 CC
     vaccine adjuvants against, C. neoformans infection, or for generating
 CC
     antigen-specific T cells. The present sequence is a human protein shown
 CC
     in the exemplification of the invention
XX
 SO
     Sequence 317 AA;
  Query Match
                       100.0%; Score 1685; DB 5; Length 317;
  Best Local Similarity
                       100.0%; Pred. No. 4.3e-154;
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Db
Qу
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Db
         181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
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Db
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    ABP55108 standard; protein; 317 AA.
XX
АC
    ABP55108;
XX
DT
    05-FEB-2003 (first entry)
XX
    Human osteoprotegerin ligand.
DE
XX
    Osteoprotegerin ligand; OPG ligand; OPGL; human; autoimmune disease;
KW
    rheumatoid arthritis; diabetes; osteoarthritis; psoriasis;
KW
    inflammatory bowel disease; transplant rejection; allergy;
KW
    immunosuppressive; antirheumatic; antiarthritic; antidiabetic;
KW
    antipsoriatic; immunosuppressive; antiallergic; antiinflammatory;
KW
KW
    osteopathic; antiulcer; monocyte.
XX
OS
    Homo sapiens.
```

CC

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XX
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                      Location/Qualifiers
      Key
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                      1. .47
FT
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XX
ΡN
     WO200276507-A2.
XX
PD
     03-OCT-2002.
XX
ΡF
     06-FEB-2002; 2002WO-US001238.
XX
PR
     23-MAR-2001; 2001US-0278215P.
XX
PΑ
     (GETH ) GENENTECH INC.
XX
PΙ
     Grewal I;
XX
DR
     WPI; 2003-058352/05.
DR
     N-PSDB; ABV75842.
XX
PT
     Stimulating mammalian monocytes by exposing to an OPG ligand polypeptide,
PT
     useful for treating immune related disorders such as autoimmune disease,
PT
     rheumatoid arthritis, diabetes, osteoarthritis, psoriasis, and allergy.
XX
PS
     Claim 1; Fig 1B; 111pp; English.
XX
CC
     The present sequence is the protein sequence of human osteoprotegerin
CC
     ligand (OPGL), a member of the tumour necrosis factor (TNF) family of
CC
     molecules that has been reported to bind to at least 2 receptors, RANK
CC
     and OPG. In the present invention, OPGL was shown to activate human
CC
     monocytes, and to activate such monocytes to secrete certain cytokines
CC
     such as interleukin-1 (IL-1), IL-6, IL-12, MIP-1alpha and TNF-alpha and
CC
     chemokines such as IL-8. OPGL may function in up-regulation of co-
     stimulatory molecules such as ICAM-a and VCAM-1, LFA, and B7.1, B7.3 and
CC
CC
     B7h. OPGL may also serve as an antigen presenting molecule which enhances
CC
     T-cell activation. The invention provides methods of using OPGL to
CC
     activate monocytes to secrete chemokines or cytokines by exposing a
     mammalian cell (in cell culture or in a mammal) to OPGL. Also provided
CC
CC
     are methods of using OPGL to treat conditions or diseases in mammals
CC
     associated with, or resulting from lack of, or decreased, chemokine or
CC
     cytokine secretion by monocytes. The invention also provides agonist and
CC
     antagonist molecules to modulate immune activity. These may include
CC
     antibodies to the OPG or RANK receptors. An antagonist comprising an anti
CC
     -OPGL antibody, an anti-OPG receptor antibody, an anti-RANK receptor
    antibody, an OPG receptor immunoadhesin or a RANK receptor immunoadhesin
CC
```

is used in a claimed method of treating an immune-related condition,

diabetes, osteoarthritis, inflammatory bowel disease (especially

especially an autoimmune disease, rheumatoid arthritis, insulin dependent

ulcerative colitis or Crohn's disease), psoriasis, transplant rejection

CC

CC

CC CC

```
CC
     or allergy
 XX
 SQ
     Sequence 317 AA;
  Query Match
                       100.0%; Score 1685; DB 6; Length 317;
  Best Local Similarity 100.0%; Pred. No. 4.3e-154;
  Matches 317; Conservative 0; Mismatches
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Qу
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Db
QУ
         181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
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XX
AC
    AAE34364;
XX
DT
    14-MAY-2003 (first entry)
XX
DE
    Human receptor activator of NF-kappa B ligand (RANKL).
XX
KW
    Human; acute septic arthritis; osteomalacia; hyperparathyroidism;
KW
    Cushing's syndrome; receptor activator of NF-kappa B ligand; cancer;
    bone formation; rickets; Langerhan's cell histiocytosis; gene therapy;
KW
    monoostotic fibrous dysplasia; radiation therapy; spinal cord injury;
KW
KW
    RANKL; Gaucher's disease; polyostotic fibrous dysplasia; scurvy.
XX
OS
    Homo sapiens.
XX
FΗ
    Key
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FT
    Domain
                 1. .47
FT
                 /note= "Intracellular domain"
FT
    Domain
                 48. .68
FT
                 /note= "Transmembrane domain"
FT
    Domain
                 69. .317
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                     162. .317
FT
                     /note= "RANK-binding domain"
XX
ΡN
     W0200292016-A2.
XX
PD
     21-NOV-2002.
XX
PF
     17-MAY-2002; 2002WO-US016002.
XX
PR
     17-MAY-2001; 2001US-0291919P.
XX
PΑ
     (IMMV) IMMUNEX CORP.
XX
ΡI
     Dougall WC, Anderson DM;
XX
DR
     WPI; 2003-129220/12.
DR
     N-PSDB; AAD52598.
XX
PT
     Treating patients having e.g. acute septic arthritis, osteomalacia,
     hyperparathyroidism, Cushing's syndrome or spinal cord injury, comprises
PT
PT
     administering a receptor activator of NF-kappa B antagonist to increase
PT
     bone formation.
XX
     Claim 1; Page 51-52; 52pp; English.
PS
XX
CC
     The invention relates to a method of treating a patient having e.g. acute
     septic arthritis, osteomalacia, hyperparathyroidism, Cushing's syndrome
CC
CC
     or spinal cord injury. The method involves administering a receptor
CC
     activator of NF-kappa B (RANK) antagonist to stimulate an increase in the
CC
     rate for formation of new bone. RANK antagonist is capable of inhibiting
CC
     the ability of RANK to induce NF-kappa B. The method is useful for
CC
     stimulating bone formation, or for treating patients having acute septic
CC
     arthritis, osteomalacia (including rickets and scurvy),
CC
    hyperparathyroidism, Cushing's syndrome, monoostotic fibrous dysplasia,
    polyostotic fibrous dysplasia, Gaucher's disease, Langerhan's cell
CC
CC
    histiocytosis, spinal cord injury, patients requiring periodontal
CC
    reconstruction, or patients who have completed a course or radiation
CC
    therapy for cancer. The method is also useful for treating a patient who
CC
    is a prosthetic joint recipient, a bone graft recipient, or a ligament
    graft recipient. The invention is useful in gene therapy. The present
CC
CC
    sequence is human RANK ligand (RANKL) protein
XX
SO
    Sequence 317 AA;
 Query Match
                        100.0%; Score 1685; DB 6; Length 317;
 Best Local Similarity
                        100.0%; Pred. No. 4.3e-154;
 Matches 317; Conservative
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Qу
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RESULT 15
ABR42314
ID
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XX
AC
    ABR42314;
XX
DТ
    11-AUG-2003 (first entry)
XX
DE
    Human RANKL protein.
XX
    Human; RANKL; tumour necrosis factor; ligand; cytostatic;
KW
KW
    immunomodulator; osteopathic.
XX
OS
    Homo sapiens.
XX
ΡN
    W02003040307-A2.
XX
PD
    15-MAY-2003.
XX
PF
    25-JUL-2002; 2002WO-US023782.
XX
PR
    27-JUL-2001; 2001US-0307838P.
XX
PΑ
    (HUMA-) HUMAN GENOME SCI INC.
XX
PΙ
    Hilbert DH, Rosen CA;
XX
DR
    WPI; 2003-430659/40.
XX
PT
    New heteromultimeric complex having a first polypeptide member of the
РΤ
    tumor necrosis factor (TNF) ligand family, and a second different member
PT
    of TNF ligand family, useful for treating cancer, osteoporosis or an
PT
    autoimmune disease.
XX
PS
    Disclosure; Page 366-367; 388pp; English.
XX
CC
    The present sequence is the protein sequence of human RANKL protein. The
CC
    invention relates to compositions comprising heterotrimeric complexes of
CC
    tumour necrosis factor (TNF) ligand family members, and their use in the
```

detection, prevention and treatment of disease. In one embodiment, the

CC

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heterotrimeric complex comprises full-length or extracellular portions of
CC
CC
    RANKL and full-length or extracellular portions of other TNF ligand
CC
    family members, preferably TRAIL. The heterotrimeric complexes of the
    invention are useful for treating an autoimmune disease, cancer or
CC
CC
    osteoporosis, and particularly for inhibiting cancer cell proliferation,
    increasing B cell proliferation, or inducing apoptosis of T cells. A
CC
    claimed method of inhibiting cancer cell proliferation comprises
CC
    administering a heterotrimeric complex consisting of TRAIL and CD40L or
CC
CC
    RANKL. A claimed method of treating osteoporosis comprises administering
CC
    an antibody against a complex comprising RANKL and TRAIL
XX
SQ
    Sequence 317 AA;
 Query Match
                      100.0%; Score 1685; DB 6; Length 317;
 Best Local Similarity
                    100.0%; Pred. No. 4.3e-154;
 Matches 317; Conservative
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Db
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OM protein - protein search, using sw model

Run on: February 25, 2004, 16:27:52; Search time 23 Seconds

(without alignments)

711.541 Million cell updates/sec

Title: US-09-787-126-2

Perfect score: 1685

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Scoring table: BLOSUM62

Gapop 10.0 , Gapext 0.5

Searched: 389414 seqs, 51625971 residues

Total number of hits satisfying chosen parameters: 389414

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%

Maximum Match 100%

Listing first 45 summaries

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SUMMARIES

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1685	100.0	317	4	US-09-052-521C-4	Sequence 4, Appli
1685	100.0	317	4	US-09-577-780-13	Sequence 13, Appl
1685	100.0	317	4	US-09-577-800-13	Sequence 13, Appl
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1685	100.0	317	4	US-09-871-856-13	Sequence 13, Appl
1685	100.0	317	4	US-09-871-291-13	Sequence 13, Appl
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1685	100.0	317	4	US-09-877-650-13	Sequence 13, Appl
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Sequence 7, Appli
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ALIGNMENTS

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; Patent No. 6017729
  GENERAL INFORMATION:
     APPLICANT: Anderson, Dirk M.
     APPLICANT: Galibert, Laurent
     APPLICANT: Maraskovsky, Eugene
     TITLE OF INVENTION: Receptor Activator of NF-kappaB
     NUMBER OF SEQUENCES: 19
     CORRESPONDENCE ADDRESS:
       ADDRESSEE: Immunex Corporation, Law Department
       STREET: 51 University Street
       CITY: Seattle
       STATE: WA
       COUNTRY: USA
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       ZIP: 98101
     COMPUTER READABLE FORM:
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MEDIUM TYPE: Floppy disk
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     COMPUTER: Apple Power Macintosh
     OPERATING SYSTEM: Apple Operating System 7.5.5
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     APPLICATION NUMBER: US/08/996,139
     FILING DATE: 22 DECEMBER 1997
     CLASSIFICATION:
    PRIOR APPLICATION DATA:
     APPLICATION NUMBER: USSN 60/064,671
     FILING DATE: 14 OCTOBER 1997
    PRIOR APPLICATION DATA:
     APPLICATION NUMBER: USSN 08/813,509
     FILING DATE: 07 MARCH 1997
    PRIOR APPLICATION DATA:
     APPLICATION NUMBER: USSN 08/772,330
     FILING DATE: 23 DECEMBER 1996
    ATTORNEY/AGENT INFORMATION:
     NAME: Perkins, Patricia Anne
     REGISTRATION NUMBER: 34,693
     REFERENCE/DOCKET NUMBER: 2851-A
    TELECOMMUNICATION INFORMATION:
     TELEPHONE: (206)587-0430
     TELEFAX: (206)233-0644
  INFORMATION FOR SEQ ID NO: 13:
    SEQUENCE CHARACTERISTICS:
      LENGTH: 317 amino acids
      TYPE: amino acid
      TOPOLOGY: linear
    MOLECULE TYPE: protein
US-08-996-139-13
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; Patent No. 6242213
  GENERAL INFORMATION:
     APPLICANT: Anderson, Dirk M.
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    APPLICANT: Galibert, Laurent APPLICANT: Maraskovsky, Eugene
    TITLE OF INVENTION: Ligand for Receptor Activator of NF-kappaB
    NUMBER OF SEQUENCES: 19
    CORRESPONDENCE ADDRESS:
      ADDRESSEE: Immunex Corporation, Law Department
       STREET: 51 University Street
      CITY: Seattle
      STATE: WA
      COUNTRY: USA
      ZIP: 98101
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       COMPUTER: Apple Power Macintosh
       OPERATING SYSTEM: Apple Operating System 7.5.5
       SOFTWARE: Microsoft Word for Power Macintosh 6.0.1
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       FILING DATE: 22 DECEMBER 1997
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       FILING DATE: 14 OCTOBER 1997
       CLASSIFICATION:
    PRIOR APPLICATION DATA:
       APPLICATION NUMBER: USSN 08/813,509
       FILING DATE: 07 MARCH 1997
      CLASSIFICATION:
     PRIOR APPLICATION DATA:
       APPLICATION NUMBER: USSN 08/772,330
       FILING DATE: 23 DECEMBER 1996
      CLASSIFICATION:
    ATTORNEY/AGENT INFORMATION:
       NAME: Perkins, Patricia Anne
       REGISTRATION NUMBER: 34,693
       REFERENCE/DOCKET NUMBER: 2852-A
     TELECOMMUNICATION INFORMATION:
       TELEPHONE: (206)587-0430
       TELEFAX: (206)233-0644
   INFORMATION FOR SEQ ID NO: 13:
     SEQUENCE CHARACTERISTICS:
       LENGTH: 317 amino acids
       TYPE: amino acid
       TOPOLOGY: linear
     MOLECULE TYPE: protein
US-08-995-659-13
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; Patent No. 6271349
   GENERAL INFORMATION:
       APPLICANT: Anderson, Dirk M.
                Galibert, Laurent
                Maraskovsky, Eugene
       TITLE OF INVENTION: Receptor Activator of NF-kappaB
       NUMBER OF SEQUENCES: 19
       CORRESPONDENCE ADDRESS:
           ADDRESSEE: Immunex Corporation, Law Department
           STREET: 51 University Street
           CITY: Seattle
           STATE: WA
           COUNTRY: USA
           ZIP: 98101
       COMPUTER READABLE FORM:
           MEDIUM TYPE: Floppy disk
           COMPUTER: Apple Power Macintosh
           OPERATING SYSTEM: Apple Operating System 7.5.5
           SOFTWARE: Microsoft Word for Power Macintosh 6.0.1
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       ATTORNEY/AGENT INFORMATION:
            NAME: Perkins, Patricia Anne
            REGISTRATION NUMBER: 34,693
            REFERENCE/DOCKET NUMBER: 2851-A
       TELECOMMUNICATION INFORMATION:
            TELEPHONE: (206) 587-0430
            TELEFAX: (206)233-0644
   INFORMATION FOR SEQ ID NO: 13:
       SEQUENCE CHARACTERISTICS:
            LENGTH: 317 amino acids
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; Patent No. 6316408
; GENERAL INFORMATION:
; APPLICANT: Boyle, William J.
; TITLE OF INVENTION: Osteoprotegerin Binding Proteins and Receptors
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  PRIOR FILING DATE: 1997-06-23
  PRIOR APPLICATION NUMBER: 08/842,842
  PRIOR FILING DATE: 1997-04-16
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; Patent No. 6419929
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       APPLICANT: Anderson, Dirk M.
                 Galibert, Laurent
                 Maraskovsky, Eugene
       TITLE OF INVENTION: Ligand for Receptor Activator of NF-kappaB
       NUMBER OF SEQUENCES: 19
       CORRESPONDENCE ADDRESS:
            ADDRESSEE: Immunex Corporation, Law Department
            STREET: 51 University Street
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CITY: Seattle
            STATE: WA
            COUNTRY: USA
            ZIP: 98101
       COMPUTER READABLE FORM:
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            CLASSIFICATION: <Unknown>
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            FILING DATE: <Unknown>
            APPLICATION NUMBER: USSN 08/813,509
            FILING DATE: 07 MARCH 1997
            APPLICATION NUMBER: USSN 08/772,330
            FILING DATE: 23 DECEMBER 1996
       ATTORNEY/AGENT INFORMATION:
            NAME: Perkins, Patricia Anne
            REGISTRATION NUMBER: 34,693
            REFERENCE/DOCKET NUMBER: 2852-A
       TELECOMMUNICATION INFORMATION:
            TELEPHONE: (206) 587-0430
            TELEFAX: (206)233-0644
   INFORMATION FOR SEQ ID NO: 13:
       SEQUENCE CHARACTERISTICS:
            LENGTH: 317 amino acids
            TYPE: amino acid
            TOPOLOGY: linear
       MOLECULE TYPE: protein
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; Patent No. 6479635
  GENERAL INFORMATION:
    APPLICANT: Anderson, Dirk M.
    APPLICANT: Galibert, Laurent
    APPLICANT: Maraskovsky, Eugene
    TITLE OF INVENTION: Receptor Activator of NF-kappaB
    NUMBER OF SEQUENCES: 19
    CORRESPONDENCE ADDRESS:
      ADDRESSEE: Immunex Corporation, Law Department
      STREET: 51 University Street
     CITY: Seattle
     STATE: WA
     COUNTRY: USA
     ZIP: 98101
    COMPUTER READABLE FORM:
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      APPLICATION NUMBER: US 08/996,139
      FILING DATE: 22 DECEMBER 1997
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      FILING DATE: 14 OCTOBER 1997
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      FILING DATE: 07 MARCH 1997
    PRIOR APPLICATION DATA:
      APPLICATION NUMBER: USSN 08/772,330
      FILING DATE: 23 DECEMBER 1996
    ATTORNEY/AGENT INFORMATION:
      NAME: Perkins, Patricia Anne
      REGISTRATION NUMBER: 34,693
      REFERENCE/DOCKET NUMBER: 2851-A
    TELECOMMUNICATION INFORMATION:
      TELEPHONE: (206) 587-0430
      TELEFAX: (206)233-0644
  INFORMATION FOR SEQ ID NO: 13:
   SEQUENCE CHARACTERISTICS:
      LENGTH: 317 amino acids
      TYPE: amino acid
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TOPOLOGY: linear
    MOLECULE TYPE: protein
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; Patent No. 6528482
   GENERAL INFORMATION:
       APPLICANT: Anderson, Dirk M.
                 Galibert, Laurent
                 Maraskovsky, Eugene
       TITLE OF INVENTION: Receptor Activator of NF-kappaB
       NUMBER OF SEQUENCES: 19
       CORRESPONDENCE ADDRESS:
           ADDRESSEE: Immunex Corporation, Law Department
            STREET: 51 University Street
            CITY: Seattle
            STATE: WA
            COUNTRY: USA
            ZIP: 98101
       COMPUTER READABLE FORM:
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           APPLICATION NUMBER: USSN 60/064,671
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           APPLICATION NUMBER: USSN 08/813,509
           FILING DATE: 07 MARCH 1997
           APPLICATION NUMBER: USSN 08/772,330
            FILING DATE: 23 DECEMBER 1996
       ATTORNEY/AGENT INFORMATION:
           NAME: Perkins, Patricia Anne
            REGISTRATION NUMBER: 34,693
           REFERENCE/DOCKET NUMBER: 2851-A
       TELECOMMUNICATION INFORMATION:
            TELEPHONE: (206)587-0430
           TELEFAX: (206) 233-0644
   INFORMATION FOR SEQ ID NO: 13:
       SEQUENCE CHARACTERISTICS:
            LENGTH: 317 amino acids
            TYPE: amino acid
           TOPOLOGY: linear
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            61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
Db
        121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
QУ
            121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
Db
        181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
Qy
            181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
Db
        241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Qу
            241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Db
        301 PDQDATYFGAFKVRDID 317
Qу
            301 PDODATYFGAFKVRDID 317
Db
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US-09-871-856-13
; Sequence 13, Application US/09871856
; Patent No. 6537763
   GENERAL INFORMATION:
        APPLICANT: Anderson, Dirk M.
                   Galibert, Laurent
                   Maraskovsky, Eugene
        TITLE OF INVENTION: Receptor Activator of NF-kappaB
        NUMBER OF SEQUENCES: 19
        CORRESPONDENCE ADDRESS:
             ADDRESSEE: Immunex Corporation, Law Department
              STREET: 51 University Street
              CITY: Seattle
              STATE: WA
              COUNTRY: USA
              ZIP: 98101
         COMPUTER READABLE FORM:
              MEDIUM TYPE: Floppy disk
              COMPUTER: Apple Power Macintosh
              OPERATING SYSTEM: Apple Operating System 7.5.5
              SOFTWARE: Microsoft Word for Power Macintosh 6.0.1
         CURRENT APPLICATION DATA:
              APPLICATION NUMBER: US/09/871,856
              FILING DATE: 31-May-2001
              CLASSIFICATION: <Unknown>
         PRIOR APPLICATION DATA:
              APPLICATION NUMBER: 08/996,139
              FILING DATE: <Unknown>
              APPLICATION NUMBER: USSN 08/813,509
              FILING DATE: 07 MARCH 1997
              APPLICATION NUMBER: USSN 08/772,330
              FILING DATE: 23 DECEMBER 1996
         ATTORNEY/AGENT INFORMATION:
              NAME: Perkins, Patricia Anne
               REGISTRATION NUMBER: 34,693
               REFERENCE/DOCKET NUMBER: 2851-A
          TELECOMMUNICATION INFORMATION:
               TELEPHONE: (206) 587-0430
               TELEFAX: (206)233-0644
     INFORMATION FOR SEQ ID NO: 13:
          SEQUENCE CHARACTERISTICS:
               LENGTH: 317 amino acids
               TYPE: amino acid
               TOPOLOGY: linear
          MOLECULE TYPE: protein
          SEQUENCE DESCRIPTION: SEQ ID NO: 13:
  US-09-871-856-13
                           100.0%; Score 1685; DB 4; Length 317;
    Query Match
                           100.0%; Pred. No. 2.6e-163;
    Best Local Similarity
                                                                             0;
                                 0; Mismatches 0; Indels
    Matches 317; Conservative
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                QУ
              1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
  Db
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  QУ
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Qу
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Db
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Qy
            181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
Db
        241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Qу
            241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Db
        301 PDQDATYFGAFKVRDID 317
Qу
            301 PDQDATYFGAFKVRDID 317
Db
RESULT 9
US-09-871-291-13
; Sequence 13, Application US/09871291
; Patent No. 6562948
   GENERAL INFORMATION:
       APPLICANT: Anderson, Dirk M.
                 Galibert, Laurent
                 Maraskovsky, Eugene
       TITLE OF INVENTION: Receptor Activator of NF-kappaB
       NUMBER OF SEQUENCES: 19
       CORRESPONDENCE ADDRESS:
            ADDRESSEE: Immunex Corporation, Law Department
            STREET: 51 University Street
            CITY: Seattle
            STATE: WA
            COUNTRY: USA
            ZIP: 98101
       COMPUTER READABLE FORM:
            MEDIUM TYPE: Floppy disk
            COMPUTER: Apple Power Macintosh
            OPERATING SYSTEM: Apple Operating System 7.5.5
            SOFTWARE: Microsoft Word for Power Macintosh 6.0.1
       CURRENT APPLICATION DATA:
            APPLICATION NUMBER: US/09/871.291
            FILING DATE: 30-May-2001
            CLASSIFICATION: <Unknown>
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            APPLICATION NUMBER: 08/996,139
            FILING DATE: <Unknown>
            APPLICATION NUMBER: USSN 08/813,509
            FILING DATE: 07 MARCH 1997
            APPLICATION NUMBER: USSN 08/772,330
            FILING DATE: 23 DECEMBER 1996
       ATTORNEY/AGENT INFORMATION:
            NAME: Perkins, Patricia Anne
            REGISTRATION NUMBER: 34,693
            REFERENCE/DOCKET NUMBER: 2851-A
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TELECOMMUNICATION INFORMATION:
;
           TELEPHONE: (206) 587-0430
;
           TELEFAX: (206) 233-0644
   INFORMATION FOR SEQ ID NO: 13:
       SEQUENCE CHARACTERISTICS:
           LENGTH: 317 amino acids
           TYPE: amino acid
           TOPOLOGY: linear
       MOLECULE TYPE: protein
       SEQUENCE DESCRIPTION: SEQ ID NO: 13:
US-09-871-291-13
                      100.0%; Score 1685; DB 4; Length 317;
 Query Match
                     100.0%; Pred. No. 2.6e-163;
 Best Local Similarity
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                          0; Mismatches
                                          0; Indels
                                                       0; Gaps
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           1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
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         61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
Qy
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            181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
Db
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Qу
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Db
        301 PDQDATYFGAFKVRDID 317
Qy
            Db
        301 PDODATYFGAFKVRDID 317
RESULT 10
US-09-396-937-2
; Sequence 2, Application US/09396937
; Patent No. 6645500
; GENERAL INFORMATION:
  APPLICANT: M&E Biotech A/S
  APPLICANT: HALKIER, Torben
  APPLICANT: HAANING, Jesper
  TITLE OF INVENTION: Method for Down-Regulating Osteoprotegerin Ligand
  TITLE OF INVENTION: Activity
  FILE REFERENCE: 22021 PC 1
  CURRENT APPLICATION NUMBER: US/09/396,937
  CURRENT FILING DATE: 1999-09-15
; NUMBER OF SEQ ID NOS: 35
 SOFTWARE: PatentIn Ver. 2.1
; SEQ ID NO 2
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LENGTH: 317
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   ORGANISM: Homo sapiens
US-09-396-937-2
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 Query Match
 Best Local Similarity 100.0%; Pred. No. 2.6e-163;
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            Db
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         61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
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Qу
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Db
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Qу
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        301 PDQDATYFGAFKVRDID 317
Qу
           301 PDQDATYFGAFKVRDID 317
Db
RESULT 11
US-09-877-650-13
; Sequence 13, Application US/09877650
: Patent No. 6649164
   GENERAL INFORMATION:
       APPLICANT: Anderson, Dirk M.
                Galibert, Laurent
;
                Maraskovsky, Eugene
       TITLE OF INVENTION: Ligand for Receptor Activator of NF-kappaB
;
       NUMBER OF SEQUENCES: 19
       CORRESPONDENCE ADDRESS:
           ADDRESSEE: Immunex Corporation, Law Department
           STREET: 51 University Street
           CITY: Seattle
           STATE: WA
           COUNTRY: USA
            ZIP: 98101
       COMPUTER READABLE FORM:
           MEDIUM TYPE: Floppy disk
           COMPUTER: Apple Power Macintosh
           OPERATING SYSTEM: Apple Operating System 7.5.5
            SOFTWARE: Microsoft Word for Power Macintosh 6.0.1
       CURRENT APPLICATION DATA:
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APPLICATION NUMBER: US/09/877,650
;
            FILING DATE: 08-Jun-2001
;
           CLASSIFICATION: <Unknown>
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       PRIOR APPLICATION DATA:
           APPLICATION NUMBER: 08/995,659
           FILING DATE: 1997-12-22
           APPLICATION NUMBER: USSN 08/813,509
           FILING DATE: 07 MARCH 1997
           APPLICATION NUMBER: USSN 08/772,330
            FILING DATE: 23 DECEMBER 1996
       ATTORNEY/AGENT INFORMATION:
           NAME: Perkins, Patricia Anne
            REGISTRATION NUMBER: 34,693
           REFERENCE/DOCKET NUMBER: 2852-A
       TELECOMMUNICATION INFORMATION:
            TELEPHONE: (206) 587-0430
           TELEFAX: (206)233-0644
   INFORMATION FOR SEQ ID NO: 13:
       SEQUENCE CHARACTERISTICS:
           LENGTH: 317 amino acids
           TYPE: amino acid
           TOPOLOGY: linear
       MOLECULE TYPE: protein
       SEQUENCE DESCRIPTION: SEQ ID NO: 13:
US-09-877-650-13
 Query Match
                      100.0%; Score 1685; DB 4; Length 317;
 Best Local Similarity
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 Matches 317; Conservative 0; Mismatches
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Db
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RESULT 12 US-08-842-842-7

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; Sequence 7, Application US/08842842
; Patent No. 5843678
    GENERAL INFORMATION:
        APPLICANT: Boyle, William J.
        TITLE OF INVENTION: OSTEOPROTEGERIN BINDING PROTEINS
        NUMBER OF SEQUENCES: 7
        CORRESPONDENCE ADDRESS:
            ADDRESSEE: Amgen Inc.
            STREET: 1840 Dehavilland Drive
           CITY: Thousand Oaks
           STATE: California
            COUNTRY: USA
            ZIP: 91230-1789
;
       COMPUTER READABLE FORM:
;
            MEDIUM TYPE: Floppy disk
            COMPUTER: IBM PC compatible
;
            OPERATING SYSTEM: PC-DOS/MS-DOS
            SOFTWARE: PatentIn Release #1.0, Version #1.30
        CURRENT APPLICATION DATA:
           APPLICATION NUMBER: US/08/842,842
            FILING DATE:
            CLASSIFICATION: 435
        ATTORNEY/AGENT INFORMATION:
            NAME: Winter, Robert B.
            REFERENCE/DOCKET NUMBER: A-451
     INFORMATION FOR SEQ ID NO: 7:
        SEQUENCE CHARACTERISTICS:
            LENGTH: 316 amino acids
            TYPE: amino acid
            TOPOLOGY: linear
        MOLECULE TYPE: protein
US-08-842-842-7
                                                84.1%; Score 1417.5; DB 2; Length 316;
   Query Match
   Best Local Similarity 84.3%; Pred. No. 4.6e-136;
   Matches 268; Conservative 16; Mismatches
                                                                                          31; Indels
                                                                                                                         3; Gaps
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Db
                   240 VYVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLL 299
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Db
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300 DPDQDATYFGAFKVRDID 317
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         299 DPDQDATYFGAFKVQDID 316
Db
RESULT 13
US-08-989-362-2
; Sequence 2, Application US/08989362
; Patent No. 6242586
  GENERAL INFORMATION:
    APPLICANT: Gorman, Daniel M.
    APPLICANT: Mattson, Jeanine D.
    TITLE OF INVENTION: Mammalian Cell Surface Antigens; Related
    TITLE OF INVENTION: Reagents
   NUMBER OF SEQUENCES: 2
    CORRESPONDENCE ADDRESS:
      ADDRESSEE: DNAX Research Institute
;
      STREET: 901 California Avenue
      CITY: Palo Alto
     STATE: California
     COUNTRY: USA
ï
     ZIP: 94304-1104
   COMPUTER READABLE FORM:
;
     MEDIUM TYPE: Floppy disk
;
      COMPUTER: IBM PC compatible
     OPERATING SYSTEM: PC-DOS/MS-DOS
     SOFTWARE: PatentIn Release #1.0, Version #1.30
   CURRENT APPLICATION DATA:
     APPLICATION NUMBER: US/08/989,362
     FILING DATE: 12-DEC-1997
;
      CLASSIFICATION: 56
   PRIOR APPLICATION DATA:
      APPLICATION NUMBER: US 60/032,846
      FILING DATE: 13-DEC-1996
   ATTORNEY/AGENT INFORMATION:
      NAME: Ching, Edwin P.
      REGISTRATION NUMBER: 34,090
      REFERENCE/DOCKET NUMBER: DX0686
     TELECOMMUNICATION INFORMATION:
       TELEPHONE: (650)852-9196
       TELEFAX: (650) 496-1204
   INFORMATION FOR SEQ ID NO: 2:
   SEQUENCE CHARACTERISTICS:
      LENGTH: 316 amino acids
       TYPE: amino acid
      TOPOLOGY: linear
     MOLECULE TYPE: protein
US-08-989-362-2
                         84.1%; Score 1417.5; DB 3; Length 316;
  Ouery Match
  Best Local Similarity 84.3%; Pred. No. 4.6e-136;
                                                                         2;
  Matches 268; Conservative 16; Mismatches 31; Indels
            1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLH-APPPPAPHQPPAASRSMFVALLGLGLGQ 59
QУ
              1 MRRASRDYGKYLRSSEEMGSGPGVPHEGPLHPAPSAPAPAPPPAASRSMFLALLGLGLGQ 60
 Db
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60 VVCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRI 119
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Db
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Qy
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Dh
        180 HKVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLM 239
Qy
           179 HKVTLSSWYHDRGWAKISNMTLSNGKLRVNQDGFYYLYANICFRHHETSGSVPTDYLQLM 238
Db
        240 VYVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLL 299
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Db
        300 DPDQDATYFGAFKVRDID 317
Qу
           11111111111111111
        299 DPDQDATYFGAFKVQDID 316
Db
RESULT 14
US-09-052-521C-2
; Sequence 2, Application US/09052521C
; Patent No. 6316408
; GENERAL INFORMATION:
  APPLICANT: Boyle, William J.
  TITLE OF INVENTION: Osteoprotegerin Binding Proteins and Receptors
  FILE REFERENCE: A-451Brv
  CURRENT APPLICATION NUMBER: US/09/052,521C
  CURRENT FILING DATE: 1998-03-30
  PRIOR APPLICATION NUMBER: 08/880,855
; PRIOR FILING DATE: 1997-06-23
  PRIOR APPLICATION NUMBER: 08/842,842
  PRIOR FILING DATE: 1997-04-16
 NUMBER OF SEQ ID NOS: 40
  SOFTWARE: PatentIn Ver. 2.1
; SEQ ID NO 2
   LENGTH: 316
   TYPE: PRT
   ORGANISM: Mouse
US-09-052-521C-2
                     84.1%; Score 1417.5; DB 4; Length 316;
  Query Match
  Best Local Similarity 84.3%; Pred. No. 4.6e-136;
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  Matches 268; Conservative 16; Mismatches
                                                    3; Gaps
                                        31; Indels
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QУ
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119 KQAFQGAVQKELQHIVGPQRFSGAPAMMEGSWLDVAQRGKPEAQPFAHLTINAASIPSGS 178
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         180 HKVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLM 239
Qγ
             179 HKVTLSSWYHDRGWAKISNMTLSNGKLRVNQDGFYYLYANICFRHHETSGSVPTDYLQLM 238
Db
         240 VYVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLL 299
QУ
             239 VYVVKTSIKIPSSHNLMKGGSTKNWSGNSEFHFYSINVGGFFKLRAGEEISIQVSNPSLL 298
Db
         300 DPDQDATYFGAFKVRDID 317
QУ
             111111111111111111111
         299 DPDQDATYFGAFKVQDID 316
Db
RESULT 15
US-09-671-658A-2
; Sequence 2, Application US/09671658A
; Patent No. 6525180
   GENERAL INFORMATION:
        APPLICANT: Gorman, Daniel M.
                  Mattson, Jeanine D.
        TITLE OF INVENTION: Mammalian Cell Surface Antigens; Related
                           Reagents
        NUMBER OF SEQUENCES: 2
        CORRESPONDENCE ADDRESS:
             ADDRESSEE: DNAX Research Institute
             STREET: 901 California Avenue
             CITY: Palo Alto
             STATE: California
             COUNTRY: USA
             ZIP: 94304-1104
        COMPUTER READABLE FORM:
             MEDIUM TYPE: Floppy disk
             COMPUTER: IBM PC compatible
             OPERATING SYSTEM: PC-DOS/MS-DOS
             SOFTWARE: PatentIn Release #1.0, Version #1.30
        CURRENT APPLICATION DATA:
             APPLICATION NUMBER: US/09/671,658A
             FILING DATE: 27-Sep-2000
             CLASSIFICATION: <Unknown>
         PRIOR APPLICATION DATA:
             APPLICATION NUMBER: US/08/989,362
             FILING DATE: 12-DEC-1997
             APPLICATION NUMBER: US 60/032,846
             FILING DATE: 13-DEC-1996
         ATTORNEY/AGENT INFORMATION:
             NAME: Ching, Edwin P.
             REGISTRATION NUMBER: 34,090
              REFERENCE/DOCKET NUMBER: DX0686
         TELECOMMUNICATION INFORMATION:
              TELEPHONE: (650)852-9196
              TELEFAX: (650)496-1204
    INFORMATION FOR SEQ ID NO: 2:
         SEQUENCE CHARACTERISTICS:
              LENGTH: 316 amino acids
              TYPE: amino acid
```

```
TOPOLOGY: linear
      MOLECULE TYPE: protein
;
       SEQUENCE DESCRIPTION: SEQ ID NO: 2:
US-09-671-658A-2
                    84.1%; Score 1417.5; DB 4; Length 316;
 Query Match
                    84.3%; Pred. No. 4.6e-136;
 Best Local Similarity
                                                            2;
 Matches 268; Conservative 16; Mismatches
                                                  3;
                                      31; Indels
         1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLH-APPPPAPHQPPAASRSMFVALLGLGLGQ 59
QУ
           1 MRRASRDYGKYLRSSEEMGSGPGVPHEGPLHPAPSAPAPAPPPAASRSMFLALLGLGLGQ 60
Db
        60 VVCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRI 119
QУ
           61 VVCSIALFLYFRAQMDPNRISEDSTHCFYRILRLHENAGLQDSTLESEDT--LPDSCRRM 118
Db
        120 KQAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGS 179
QУ
           119 KQAFQGAVQKELQHIVGPQRFSGAPAMMEGSWLDVAQRGKPEAQPFAHLTINAASIPSGS 178
Db
        180 HKVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLM 239
Qy
           179 HKVTLSSWYHDRGWAKISNMTLSNGKLRVNQDGFYYLYANICFRHHETSGSVPTDYLQLM 238
Db
        240 VYVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLL 299
Qу
           239 VYVVKTSIKIPSSHNLMKGGSTKNWSGNSEFHFYSINVGGFFKLRAGEEISIQVSNPSLL 298
Db
        300 DPDQDATYFGAFKVRDID 317
Qу
           1111111111111
        299 DPDQDATYFGAFKVQDID 316
Db
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Search completed: February 25, 2004, 16:31:35

Job time : 25 secs

GenCore version 5.1.6 Copyright (c) 1993 - 2004 Compugen Ltd.

OM protein - protein search, using sw model

Run on: February 25, 2004, 16:25:52; Search time 20 Seconds

(without alignments)

1524.636 Million cell updates/sec

Title: US-09-787-126-2

Perfect score: 1685

Sequence: 1 MRRASRDYTKYLRGSEEMGG.....LLDPDQDATYFGAFKVRDID 317

Scoring table: BLOSUM62

Gapop 10.0 , Gapext 0.5

Searched: 283366 seqs, 96191526 residues

Total number of hits satisfying chosen parameters: 283366

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%

Maximum Match 100%

Listing first 45 summaries

Database: PIR_78:*

1: pir1:*

2: pir2:*

3: pir3:*

4: pir4:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1 2 3 4 5 6 7 8 9 10 11 12 13	189 184.5 176.5 175.5 158.5 141.5 141 137 133 132.5 131.5 130.5	11.2 10.9 10.5 10.4 9.4 8.4 8.4 8.1 7.9 7.9 7.8 7.7	281 279 261 278 261 235 234 234 233 235 235 306 233	2 2 2 2 2 2 1 1 1 2 2 2	138707 A53062 S53090 A49266 I53476 QWMSN A25451 JH0529 QWHUN I54490 JU0029 I49139 S22052	Fas ligand - human Fas ligand - mouse CD40 ligand - rat CD40 ligand - huma tumor necrosis fac

			004		
14	128	7.6	234	1	JQ1344
15	126.5	7.5	233	1	S24642
16	126	7.5	232	1	S12606
17	125.5	7.4	185	2	S52715
18	122	7.2	193	2	S06192
19	120	7.1	260	2	S21738
20	117	6.9	233	2	S11688
21	117	6.9	244	2	A46066
22	97.5	5.8	1464	1	CGHU1S
23	94.5	5.6	664	2	C84747
24	92.5	5.5	205	1	QWHUX
25	92.5	5.5	450	2	s38114
26	91.5	5.4	3848	2	T17414
27	91	5.4	493	2	AC0937
28	90.5	5.4	1694	2	S50065
29	90	5.3	730	2	JC1456
30	89.5	5.3	331	2	AF3526
31	89.5	5.3	379	2	A47659
32	89	5.3	202	1	B27303
33	89	5.3	440	2	149681
34	89	5.3	479	2	A25052
35	89	5.3	639	2	C83624
36	88.5	5.3	565	2	C89893
37	88.5	5.3	578	2	s51379
38	88.5	5.3	684	2	T01267
39	88.5	5.3	883	2	A49733
40	87.5	5.2	610	2	T06690
41	87.5	5.2	1466	1	CGHU7L
42	87	5.2	639	2	A32935
43	87	5.2	1114	2	JH0284
44	87	5.2	1315	2	G96722
45	86.5	5.1	279	2	F72339

tumor necrosis fac CD40 ligand - mous tumor necrosis fac lymphotoxin beta collagen alpha 1(I probable protein k lymphotoxin alpha hypothetical prote TipC protein - sli probable GntR-fami sialoadhesin - mou gelatinase B (EC 3 homoprotocatechuat farnesyl-protein t tumor necrosis fac glyceraldehyde-3-p fibrinogen beta ch probable two-compo hypothetical prote probable phosphoes leucine-rich repea [heparan sulfate]galactonolactone d collagen alpha 1(I protein P1 - Entam 125K surface antig hypothetical prote hypothetical prote

ALIGNMENTS

```
RESULT 1
I38707
Fas ligand - human
C; Species: Homo sapiens (man)
C; Date: 29-May-1998 #sequence_revision 29-May-1998 #text_change 21-Jul-2000
C; Accession: I38707; JC2340; S57565; I38554
R; Takahashi, T.; Tanaka, M.; Inazawa, J.; Abe, T.; Suda, T.; Nagata, S.
Int. Immunol. 6, 1567-1574, 1994
```

A; Title: Human Fas ligand: gene structure, chromosomal location and species specificity.

A; Reference number: I38707; MUID:95127560; PMID:7826947

A; Accession: I38707

A; Status: preliminary; translated from GB/EMBL/DDBJ

A; Molecule type: mRNA A; Residues: 1-281 < RES>

A;Cross-references: EMBL:U11821; NID:g595430; PIDN:AAC50124.1; PID:g595431 R;Mita, E.; Hayashi, N.; Iio, S.; Takehara, T.; Hijioka, T.; Kasahara, A.;

Fusamoto, H.; Kamada, T. Biochem. Biophys. Res. Commun. 204, 468-474, 1994

A; Title: Role of Fas ligand in apoptosis induced by hepatitis C virus infection.

```
A; Reference number: JC2340; MUID: 95071350; PMID: 7980502
A; Accession: JC2340
A; Molecule type: DNA
A; Residues: 1-281 <MIT>
A; Cross-references: GB: D38122; DDBJ: D29820; NID: g601892; PIDN: BAA07320.1;
PID:q1369902
R; Schatzlein, C.E.
submitted to the EMBL Data Library, June 1995
A; Reference number: $57565
A; Accession: S57565
A; Status: preliminary
A; Molecule type: mRNA
A; Residues: 1-281 <SCH>
A; Cross-references: EMBL: X89102; NID: g887455; PID: g887456
R; Alderson, M.R.; Tough, T.W.; Davis-Smith, T.; Braddy, S.; Falk, B.; Schooley,
K.A.; Goodwin, R.G.; Smith, C.A.; Ramsdell, F.; Lynch, D.H.
J. Exp. Med. 181, 71-77, 1995
A; Title: Fas ligand mediates activation-induced cell death in human T
lymphocytes.
A; Reference number: I38554; MUID: 95105731; PMID: 7528780
A; Accession: I38554
A; Status: preliminary; translated from GB/EMBL/DDBJ
A; Molecule type: mRNA
A; Residues: 1-281 < RE2>
A; Cross-references: EMBL: U08137; NID: g624627; PIDN: AAC50071.1; PID: g624628
C; Genetics:
A;Gene: FasL
A; Introns: 151/1; 116/3
C; Keywords: glycoprotein; transmembrane protein
F;80-102/Domain: transmembrane #status predicted <TMM>
F;76,184,250,260/Binding site: carbohydrate (Asn) (covalent) #status predicted
                       11.2%; Score 189; DB 2; Length 281;
  Ouery Match
  Best Local Similarity 21.7%; Pred. No. 1.9e-08;
  Matches 69; Conservative 43; Mismatches 98; Indels 108; Gaps
          22 PGAPHEGPLHAPPPPAP----HQPPAASRS------MFVALLGLGLGQVVCS 63
QУ
             46 PPPPPPPPLPPPPPPPPLPPLPPLKKRGNHSTGLCLLVMFFMVLVALVGLGLG----- 100
Db
         64 VALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIKQAF 123
QУ
                                    | |: :::| :
              :1 1 1
         101 --MFQLFHLQ------ 124
Db
         124 QGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLT--INATDIPSGSHK 181
QУ
                                 | | : | | | | : : |
              :::1:: |
         125 -SSLEKQIGH------ 159
         182 VSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMVY 241
 Qу
              160 ---LEWEDTYGIVLLSGVKYKKGGLVINETGLYFVYSKVYFRGQSCNN-----LPLSHK 210
 Db
         242 VTKTSIKIPSSHTLMKGGSTKY-----WSGNSEFHFYSINVGGFFKLRSGEEISIEVSN 295
 QУ
             | : | | : | | | : : | |
         211 VYMRNSKYPQDLVMMEGKMMSYCTTGQMWARSS-----YLGAVFNLTSADHLYVNVSE 263
 Db
         296 PSLLDPDQDATYFGAFKV 313
 Qy
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C:Accession: S53090

```
RESULT 2
A53062
Fas ligand - mouse
C; Species: Mus musculus (house mouse)
C; Date: 06-Jan-1995 #sequence revision 06-Jan-1995 #text_change 05-Nov-1999
C; Accession: A53062
R; Takahashi, T.; Tanaka, M.; Brannan, C.I.; Jenkins, N.A.; Copeland, N.G.; Suda,
T.; Nagata, S.
Cell 76, 969-976, 1994
A; Title: Generalized lymphoproliferative disease in mice, caused by a point
mutation in the Fas ligand.
A; Reference number: A53062; MUID: 94185175; PMID: 7511063
A; Accession: A53062
A; Status: preliminary
A; Molecule type: mRNA
A; Residues: 1-279 <TAK>
A; Cross-references: GB: U06948; NID: g473564; PIDN: AAA17800.1; PID: g473565
                      10.9%; Score 184.5; DB 2; Length 279;
 Query Match
 Best Local Similarity 21.7%; Pred. No. 4.6e-08;
 Matches 70; Conservative 45; Mismatches 106; Indels 101; Gaps 11;
         13 RGSEEMGGGPGAPHEGPLHAPPPPAPHQP-----PAASRSMFVALLGLGL 57
Qу
           38 RGPDQRRPPPPPPVSPLPPPSQPLPLPPLTPLKKKDHNTNLWLPVVFFMVLVALVGMGL 97
Db
         58 GQVVCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCR 117
QУ
                         :|:: |
         98 G----- 105
Db
        118 RIKQAFQGAVQKELQHI--VGSQHIRA---EKAMVDGSWLDLAKRSKLEAQPFAHLTINA 172
QΥ
                    106 -----QKELAELREFTNQSLKVSSFEKQIANPS----TPSEKKEPRSVAHLTGN- 150
Db
        173 TDIPSGSHKVSLS-SWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDL 231
Qу
                 151 -----PHSRSIPLEWEDTYGTALISGVKYKKGGLVINETGLYFVYSKVYFRGQSCN--- 201
Db
         232 ATEYLQLMVYVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISI 291
QУ
             202 -NQPLNHKVYMRNS--KYPEDLVLMEEKRLNYCT-TGQIWAHSSYLGAVFNLTSADHLYV 257
Db
         292 EVSNPSLLDPDQDATYFGAFKV 313
QУ
             :| ||:: :: |:|| :|:
         258 NISQLSLINFEESKTFFGLYKL 279
Db
RESULT 3
S53090
CD40 ligand - bovine
C; Species: Bos primigenius taurus (cattle)
C;Date: 08-Jul-1995 #sequence_revision 21-Jul-1995 #text change 05-Nov-1999
```

```
R; Mertens, B.E.L.C.; Muriuki, M.
submitted to the EMBL Data Library, February 1995
A; Description: Cloning of bovine CD40L and homology to bovine TNFA and TNFB.
A; Reference number: S53090
A; Accession: S53090
A; Status: preliminary
A; Molecule type: mRNA
A; Residues: 1-261 <MER>
A;Cross-references: EMBL:Z48469; NID:g732569; PIDN:CAA88363.1; PID:g732570
                        10.5%; Score 176.5; DB 2; Length 261;
 Query Match
 Best Local Similarity 24.2%; Pred. No. 2e-07;
 Matches 70; Conservative 54; Mismatches 122; Indels
                                                           43; Gaps
                                                                      13;
          33 PPPPAPHQPPAASRSMFVALLGLGL-GQVVCSVALFFYFRAQMDPNRISEDGTHCIYRIL 91
QУ
                    8 PSPRSVATGPPVSMKIFMYLLTVFLITQMIGSALFAVYLHRRLD--KIEDE-----R 57
Db
          92 RLHENADFQDT--TLESQDTKLIPDSCRRIKQAFQGAVQKELQHIVGSQHIRAEKAMVDG 149
Qу
              111: 1 1 : 1: 1: 1: 1:
                                                       :: :: :: :
          58 NLHEDFVFMKTIQRCNKGEGSLSLLNCEEIRSRFEDLVKDIMQ----NKEVKKKEKNFE- 112
Db
         150 SWLDLAKRSKLEAQPFAHLTINATDIPSGSHKVSLSSWYHDRGWAKISN--MTFSNGK-L 206
Qу
                   : | | | | : | : | : : : : : : : : | | | |
         113 ----MHKGDQEPQIAAHVISEAS----SKTTSVLQW-APKGYYTLSNNLVTLENGKQL 161
Db
         207 IVNQDGFYYLYANICFRHHETSGDLATEYLQLMVYVTKTSIKIP--SSHTLMKGGSTKYW 264
Qу
              162 AVKRQGFYYIYTQVTFCSNR-----ETLSQAPFIASLCLKSPSGSERILLRAANTH-- 212
Db
         265 SGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLDPDQDATYFGAFKV 313
QУ
                                                1 11 1:
                    213 SSSKPCGQQSIHLGGVFELQSGASVFVNVTDPSQVSHGTGFTSFGLLKL 261
Db
RESULT 4
A49266
fas ligand - rat
C; Species: Rattus norvegicus (Norway rat)
C;Date: 13-Jan-1995 #sequence revision 13-Jan-1995 #text change 05-Nov-1999
C; Accession: A49266
R; Suda, T.; Takahashi, T.; Golstein, P.; Nagata, S.
Cell 75, 1169-1178, 1993
A; Title: Molecular cloning and expression of the Fas ligand, a novel member of
the tumor necrosis factor family.
A; Reference number: A49266; MUID: 94084792; PMID: 7505205
A; Accession: A49266
A; Status: preliminary
A; Molecule type: mRNA
A; Residues: 1-278 <SUD>
A; Cross-references: GB: U03470; NID: g440178; PIDN: AAC52129.1; PID: g440179
C; Keywords: glycoprotein; transmembrane protein
                        10.4%; Score 175.5; DB 2; Length 278;
  Query Match
  Best Local Similarity 20.3%; Pred. No. 2.7e-07;
                                                                       10;
  Matches 64; Conservative 47; Mismatches 106; Indels 99; Gaps
```

```
21 GPGAPHEGPLHAPPPPAPHQPPAASRSM----FVALLGLGL 57
Qу
            111 | 1111:1 | 11:
                                                            |||:|:||
          39 GPGQRRPPP--PPPPPSPLPPPSQPPPLPPLSPLKKKDNIELWLPVIFFMVLVALVGMGL 96
Db
          58 GQVVCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCR 117
Qу
                   -:: | |: : : | |:|: : : | |:: : : |
          97 G-----MYQLFHLQKELAELREFTNHSL-RVSSFEKQIANPSTPSETKKPRSV----- 143
Db
         118 RIKQAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPS 177
Qy
         144 -----AHLTGNPR---- 151
Db
         178 GSHKVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQ 237
Qу
              152 -SRSIPL-EWEDTYGTALISGVKYKKGGLVINEAGLYFVYSKVYFRGQSCN----SQPLS 205
Db
         238 LMVYVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPS 297
Qу
               206 HKVYM--RNFKYPGDLVLMEEKKLNYCT-TGQIWAHSSYLGAVFNLTVADHLYVNISQLS 262
Db
         298 LLDPDQDATYFGAFKV 313
QУ
             1:: :: |:|| :|:
         263 LINFEESKTFFGLYKL 278
Db
RESULT 5
I53476
CD40 ligand - human
N; Alternate names: glycoprotein 39; hCD40-L protein; T-cell antigen gp39; TRAP
C; Species: Homo sapiens (man)
C;Date: 02-Jul-1996 #sequence_revision 02-Jul-1996 #text change 20-Apr-2001
C; Accession: S28017; JH0793; S26694; S28852; I53476; S25684; S30593
R; Hollenbaugh, D.; Grosmaire, L.S.; Kullas, C.D.; Chalupny, N.J.; Braesch-
Andersen, S.; Noelle, R.J.; Stamenkovic, I.; Ledbetter, J.A.; Aruffo, A.
EMBO J. 11, 4313-4321, 1992
A; Title: The human T cell antigen gp39, a member of the TNF gene family, is a
ligand for the CD40 receptor: expression of a soluble form of gp39 with B cell
co-stimulatory activity.
A; Reference number: S28017; MUID: 93049181; PMID: 1385114
A; Accession: S28017
A; Molecule type: mRNA
A; Residues: 1-261 <HOL>
A; Cross-references: EMBL: Z15017; NID: g38483; PIDN: CAA78737.1; PID: g38484
R; Spriggs, M.K.; Armitage, R.J.; Strockbine, L.; Clifford, K.N.; Macduff, B.M.;
Sato, T.A.; Maliszewski, C.R.; Fanslow, W.C.
J. Exp. Med. 176, 1543-1550, 1992
A; Title: Recombinant human CD40 ligand stimulates B cell proliferation and
immunoglobulin E secretion.
A; Reference number: JH0793; MUID: 93094757; PMID: 1281209
A; Accession: JH0793
A; Molecule type: mRNA
A; Residues: 1-261 <SPR>
A; Cross-references: GB: X67878; NID: g38411; PIDN: CAA48077.1; PID: g38412
A; Experimental source: peripheral blood T-cell
R; Graf, D.; Korthaeuer, U.; Mages, H.W.; Senger, G.; Kroczek, R.A.
Eur. J. Immunol. 22, 3191-3194, 1992
```

```
A; Title: Cloning of TRAP, a ligand for CD40 on human T cells.
A; Reference number: S26694; MUID: 93076854; PMID: 1280226
A; Accession: S26694
A; Status: preliminary
A; Molecule type: mRNA
A; Residues: 1-261 <GRA>
A; Cross-references: EMBL: X68550; NID: g37269; PIDN: CAA48554.1; PID: g37270
R; Gauchat, J.F.; Aubry, J.P.; Mazzei, G.; Life, P.; Jomotte, T.; Elson, G.;
Bonnefoy, J.Y.
FEBS Lett. 315, 259-266, 1993
A; Title: Human CD40-ligand: molecular cloning, cellular distribution and
regulation of expression by factors controlling IgE production.
A; Reference number: S28852; MUID: 93138085; PMID: 7678552
A; Accession: S28852
A; Molecule type: mRNA
A; Residues: 1-261 <GAU>
A; Cross-references: EMBL:L07414; NID:g180123; PIDN:AAA35662.1; PID:g180124
A; Note: the sequence from Fig. 3 is inconsistent with that from Fig. 2 in having
6-Gln
C; Genetics:
A; Gene: GDB:CD40LG; HIGM1; IMD3
A; Cross-references: GDB:120632; OMIM:308230
A; Map position: Xq26-Xq26
C; Keywords: glycoprotein; transmembrane protein
F;13-44/Domain: transmembrane #status predicted <TMM>
F;45-261/Domain: extracellular #status predicted <EXT>
F; 6, 240/Binding site: carbohydrate (Asn) (covalent) #status predicted
  Query Match 9.4%; Score 158.5; DB 2; Length 261; Best Local Similarity 24.5%; Pred. No. 6.8e-06;
          68; Conservative 53; Mismatches 113; Indels 43; Gaps
  Matches
          45 SRSMFVALLGLGL-GQVVCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDT- 102
Qу
             | | | | : | | | |
          20 SMKIFMYLLTVFLITQMIGSALFAVYLHRRLD--KIEDE-----RNLHEDFVFMKTI 69
Db
          103 -TLESQDTKLIPDSCRRIKQAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLE 161
Qу
                                            : |: : |: :: | :
                 70 QRCNTGERSLSLLNCEEIKSQFEGFV-KDIM-----LNKEETKKENSF-EMQKGDQ-N 119
Db
          162 AQPFAHLTINATDIPSGSHKVSLSSWYHDRGWAKISN--MTFSNGK-LIVNQDGFYYLYA 218
QУ
               120 PQIAAHVISEAS----SKTTSVLQW-AEKGYYTMSNNLVTLENGKQLTVKRQGLYYIYA 173
Db
          219 NICFRHHETSGDLATEYLQLMVYVTKTSIKIPS--SHTLMKGGSTKYWSGNSEFHFYSIN 276
QУ
               : | : : | :: :| | :: :| |
          174 QVTFCSNREASSQAP-----FIASLCLKSPGRFERILLRAANTH--SSAKPCGQQSIH 224
Db
          277 VGGFFKLRSGEEISIEVSNPSLLDPDQDATYFGAFKV 313
Qу
              225 LGGVFELQPGASVFVNVTDPSQVSHGTGFTSFGLLKL 261
Db
RESULT 6
QWMSN
 tumor necrosis factor alpha precursor - mouse
N; Alternate names: cachectin; TNF alpha
```

C; Species: Mus musculus (house mouse) C;Date: 31-Mar-1988 #sequence_revision 31-Mar-1988 #text_change 04-Feb-2000 C; Accession: A22908; S03791; A27303; A25164; A23127; A34251; I59058; A36696 R; Shirai, T.; Shimizu, N.; Shiojiri, S.; Horiguchi, S.; Ito, H. DNA 7, 193-201, 1988 A; Title: Cloning and expression in Escherichia coli of the gene for mouse tumor necrosis factor. A; Reference number: A22908; MUID: 88224564; PMID: 2836146 A; Accession: A22908 A; Molecule type: DNA A; Residues: 1-235 <SHI> A; Cross-references: GB:M20155 R; Shakhov, A.N.; Nedospasov, S.A. Bioorg. Khim. 13, 701-705, 1987 A; Title: Molecular cloning of the genes coding for tumor necrosis factors: complete nucleotide sequence of the genomic copy of TNF-alpha in mice. A; Reference number: S03791; MUID: 87298639; PMID: 3040015 A; Accession: S03791 A; Molecule type: DNA A; Residues: 1-235 <SHA> A;Cross-references: GB:M38296; NID:g202086; PIDN:AAA40459.1; PID:g202087 A; Note: article in Russian with English abstract R; Semon, D.; Kawashima, E.; Jongeneel, C.V.; Shakhov, A.N.; Nedospasov, S.A. Nucleic Acids Res. 15, 9083-9084, 1987 A; Title: Nucleotide sequence of the murine TNF locus, including the TNF-alpha-(tumor necrosis factor) and TNF-beta-(lymphotoxin) genes. A; Reference number: A93679; MUID: 88067722; PMID: 3684584 A; Accession: A27303 A; Molecule type: DNA A; Residues: 1-235 <SEM> A; Cross-references: GB: Y00467; NID: g54830; PIDN: CAA68530.1; PID: q54832 R; Pennica, D.; Hayflick, J.S.; Bringman, T.S.; Palladino, M.A.; Goeddel, D.V. Proc. Natl. Acad. Sci. U.S.A. 82, 6060-6064, 1985 A; Title: Cloning and expression in Escherichia coli of the cDNA for murine tumor necrosis factor. A; Reference number: A25164; MUID: 85298296; PMID: 3898078 A; Accession: A25164 A; Molecule type: mRNA A; Residues: 1-235 < PEN> A; Cross-references: GB:M11731; NID:g202084; PIDN:AAA40458.1; PID:g202085 R; Fransen, L.; Muller, R.; Marmenout, A.; Tavernier, J.; van der Heyden, J.; Kawashima, E.; Chollet, A.; Tizard, R.; van Heuverswyn, H.; van Vliet, A.; Ruysschaert, M.R.; Fiers, W. Nucleic Acids Res. 13, 4417-4429, 1985 A; Title: Molecular cloning of mouse tumour necrosis factor cDNA and its eukaryotic expression. A; Reference number: A23127; MUID: 85242112; PMID: 2989794 A; Accession: A23127 A; Molecule type: mRNA A: Residues: 1-235 <FRA> A; Cross-references: GB: X02611; NID: g54844; PIDN: CAA26457.1; PID: g54845 R; Cseh, K.; Beutler, B. J. Biol. Chem. 264, 16256-16260, 1989 A; Title: Alternative cleavage of the cachectin/tumor necrosis factor propeptide results in a larger, inactive form of secreted protein. A; Reference number: A34251; MUID: 89380231; PMID: 2777790

A; Accession: A34251

```
A; Molecule type: protein
A; Residues: 70-87 <CSE>
R; Caput, D.; Beutler, B.; Hartog, K.; Thayer, R.; Brown-Shimer, S.L.; Cerami, A.
Proc. Natl. Acad. Sci. U.S.A. 83, 1670-1674, 1986
A; Title: Identification of a common nucleotide sequence in the 3'-untranslated
region of mRNA molecules specifying inflammatory mediators.
A; Reference number: I59058; MUID: 86149365; PMID: 2419912
A; Accession: I59058
A; Status: preliminary; translated from GB/EMBL/DDBJ
A; Molecule type: mRNA
A; Residues: 1-230, 'R', 232-235 < RES>
A; Cross-references: GB:M13049; NID:g202082; PIDN:AAA40457.1; PID:g202083
R; Sherry, B.; Jue, D.M.; Zentella, A.; Cerami, A.
Biochem. Biophys. Res. Commun. 173, 1072-1078, 1990
A; Title: Characterization of high molecular weight glycosylated forms of murine
tumor necrosis factor.
A; Reference number: A36696; MUID: 91097531; PMID: 2268312
A; Accession: A36696
A; Molecule type: protein
A; Residues: 80-85, 'X', 87-99 <SHE>
C: Genetics:
A; Introns: 62/3; 81/1; 97/1
A; Note: the first intron occurs in the 5'-untranslated region
C; Superfamily: tumor necrosis factor
C; Keywords: cytokine; cytotoxin; glycoprotein; lipoprotein; lymphokine;
macrophage; membrane protein; myristylation
F;80-235/Product: tumor necrosis factor #status experimental <MAT>
F;20/Binding site: myristate (Lys) (covalent) #status predicted
F;84/Binding site: carbohydrate (Ser) (covalent) #status predicted
F;86/Binding site: carbohydrate (Asn) (covalent) #status predicted
F;148-179/Disulfide bonds: #status predicted
                          8.4%; Score 141.5; DB 1; Length 235;
  Query Match
  Best Local Similarity 25.9%; Pred. No. 0.00017;
          42; Conservative 28; Mismatches 57; Indels 35; Gaps
                                                                            7;
  Matches
          163 QPFAHLTINATDIPSGSHKVSLS-SWYHDRGWAKISN-MTFSNGKLIVNQDGFYYLYANI 220
Qу
                                   1:1
              : 1 | 1 : 1
           90 KPVAHVVAN-----HQVEEQLEWLSQRANALLANGMDLKDNQLVVPADGLYLVYSQV 141
Db
          221 CFRHHETSGDLATEYLQLMVYVTK-----TSIKIPSSHTLMKGGSTKYWSGNS 268
Qу
                                                 :::| |
                                                             : 1 | 1
                          :1: | |::
                    142 LFK-----GQGCPDYVLLTHTVSRFAISYQEKVNLLSAVKSPCPKDTPEGAELKPW---- 192
Db
          269 EFHFYSINVGGFFKLRSGEEISIEVSNPSLLD-PDQDATYFG 309
QУ
               : | :|| |:| |:::| ||: |
          193 ---YEPIYLGGVFQLEKGDQLSAEVNLPKYLDFAESGQVYFG 231
Db
RESULT 7
tumor necrosis factor alpha precursor - rabbit
N; Alternate names: cachectin; TNF alpha
C; Species: Oryctolagus cuniculus (domestic rabbit)
C;Date: 10-Sep-1999 #sequence_revision 10-Sep-1999 #text_change 04-Feb-2000
C; Accession: A25454; A25451; JS0727
```

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R; Ito, H.; Yamamoto, S.; Kuroda, S.; Sakamoto, H.; Kajihara, J.; Kiyota, T.;
Hayashi, H.; Kato, M.; Seko, M.
DNA 5, 149-156, 1986
A; Title: Molecular cloning and expression in Escherichia coli of the cDNA coding
for rabbit tumor necrosis factor.
A; Reference number: A25454; MUID: 86219711; PMID: 3519137
A; Accession: A25454
A; Molecule type: mRNA
A; Residues: 1-234 <ITO>
A;Cross-references: GB:M12845; NID:g165759; PIDN:AAA31486.1; PID:g165760
R; Ito, H.; Shirai, T.; Yamamoto, S.; Akira, M.; Kawahara, S.; Todd, C.W.;
Wallace, R.B.
DNA 5, 157-165, 1986
A; Title: Molecular cloning of the gene encoding rabbit tumor necrosis factor.
A; Reference number: A25451; MUID: 86219712; PMID: 3519138
A; Accession: A25451
A; Molecule type: DNA
A; Residues: 1-234 <IT2>
A; Note: this sequence differs from that shown in having a Gln inserted between
residues 62 and 63
R; Shakhov, A.N.; Kuprash, D.V.; Azizov, M.M.; Jongeneel, C.V.; Nedospasov, S.A.
Gene 95, 215-221, 1990
A; Title: Structural analysis of the rabbit TNF locus, containing the genes
encoding TNF-beta (lymphotoxin) and TNF-alpha (tumor necrosis factor).
A; Reference number: JH0309; MUID: 91065534; PMID: 2249779
A; Accession: JS0727
A; Status: nucleic acid sequence not shown; translation not shown
A; Molecule type: DNA
A; Residues: 1-62, 'Q', 63-234 <SHA>
A;Cross-references: GB:M60340; GB:M35326; NID:g165754; PIDN:AAA31484.1;
PID:q165756
C; Genetics:
A; Introns: 62/3; 80/1; 96/1
C; Superfamily: tumor necrosis factor
C; Keywords: cytokine; cytotoxin; glycoprotein; lipoprotein; lymphokine;
macrophage; membrane protein; myristylation
F;1-81/Domain: propeptide #status predicted <PRO>
F;82-234/Product: tumor necrosis factor #status predicted <MAT>
F;19,20/Binding site: myristate (Lys) (covalent) #status predicted
F;83/Binding site: carbohydrate (Ser) (covalent) #status predicted
F:147-178/Disulfide bonds: #status predicted
                        8.4%; Score 141; DB 1; Length 234;
  Query Match
  Best Local Similarity 21.6%; Pred. No. 0.00018;
  Matches 65; Conservative 35; Mismatches 99; Indels 102; Gaps
          27 EGPLHAPPPPAPHQPPAASR----SMFVALLGLGLGQVVCSVALFFYFRAQMDPNRISED 82
QУ
             14 EGPL----PKKAGGPQGSKRCLCLSLFSFLLVAGATTLFC----LLHFRVIGPQEEESPN 65
Db
          83 GTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIKQAFQGAVQKELQHIVGSQHIRA 142
QУ
          Db
         143 EKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSHKVSLSSWYHDRGWAKISN-MTF 201
Qу
              83 SRALSD-----KPLAHVVAN----PQVEGQL---QWLSQRANALLANGMKL 121
Db
```

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202 SNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMVYVTKTSIKIPSSHTLMKG--- 258
Qу
                                               1: | |:: :: |:
              :: :|:| || || :|: : |
                                       122 TDNQLVVPADGLYLIYSQVLF----SGQGCRSYVLLTHTVSRFAVSYPNKVNLLSAIKS 176
Db
          259 -----GSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD-PDQDATYF 308
Qy
                                    : | :|| |:| |: :| ||: | || :
                            177 PCHRETPEEAEPMAW-----YEPIYLGGVFQLEKGDRLSTEVNQPEYLDLAESGQVYF 229
Db
          309 G 309
Qу
          230 G 230
Db
RESULT 8
JH0529
tumor necrosis factor alpha precursor - sheep
N; Alternate names: cachectin; TNF alpha
C; Species: Ovis orientalis aries, Ovis ammon aries (domestic sheep)
C;Date: 10-Sep-1999 #sequence revision 10-Sep-1999 #text change 04-Feb-2000
C; Accession: JH0529; S48118; S13114; S20661
R; Green, I.R.; Sargan, D.R.
Gene 109, 203-210, 1991
A; Title: Sequence of the cDNA encoding ovine tumor necrosis factor-alpha:
problems with cloning by inverse PCR.
A; Reference number: JH0529; MUID: 92112044; PMID: 1765267
A; Accession: JH0529
A; Molecule type: mRNA
A; Residues: 1-234 <GRE>
A;Cross-references: EMBL:X55152; NID:g1405; PIDN:CAA38952.1; PID:g1406
A; Experimental source: alveolar macrophage
R; Nash, A.D.; Barcham, G.J.; Brandon, M.R.; Andrews, A.E.
Immunol. Cell Biol. 69, 273-283, 1991
A; Title: Molecular cloning, expression and characterization of ovine TNF-alpha.
A; Reference number: S48118; MUID: 92155784; PMID: 1786996
A:Accession: S48118
A; Status: preliminary
A; Molecule type: mRNA
A; Residues: 1-234 < NAS>
A;Cross-references: EMBL:X56756; NID:g297806; PIDN:CAA40076.1; PID:g297807
R; Young, A.J.; Hay, J.B.; Chan, J.Y.C.
Nucleic Acids Res. 18, 6723, 1990
A; Title: Primary structure of ovine tumor necrosis factor alpha cDNA.
A; Reference number: S13114; MUID: 91067496; PMID: 2251151
A; Accession: S13114
A; Status: preliminary
A; Molecule type: mRNA
A; Residues: 1-62,64-234 < YOU>
A; Cross-references: EMBL: X55966; NID: g1403; PIDN: CAA39437.1; PID: g1404
A; Note: comparison with the introns of homologous sequences suggest that this is
probably an alternative splicing
C; Superfamily: tumor necrosis factor
C; Keywords: alternative splicing; cytokine; cytotoxin; glycoprotein;
lipoprotein; lymphokine; macrophage; myristylation; transmembrane protein
F;1-77/Domain: propeptide #status predicted <PRO>
F;78-234/Product: tumor necrosis factor alpha #status predicted <TUM>
F;20/Binding site: myristate (Lys) (covalent) #status predicted
```

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F;96/Binding site: carbohydrate (Asn) (covalent) #status predicted
F;146-178/Disulfide bonds: #status predicted
 Query Match 8.1%; Score 137; DB 1; Length 234; Best Local Similarity 26.1%; Pred. No. 0.0004;
          52; Conservative 30; Mismatches 71; Indels 46; Gaps
                                                                         10;
         134 IVGSQHIRAEKAMVDGSW---LDLAKRSKLEA---QPFAHLTINATDIPSGSHKVSLSSW 187
QУ
             ::| | | |:: |: | | |:| |:| |:|
          55 VIGPQ--REEQSPAGPSFNRPLVQTLRSSSQASNNKPVAHVVAN-----ISAP 100
Db
         188 YHDRGWAKISNMTFSNG-----KLIVNQDGFYYLYANICFRHH-----ETSGDL 231
Qу
                101 GQLRWGDSYANALMANGVELKDNQLVVPTDGLYLIYSQVLFRGHGCPSTPLFLTHTISRI 160
Db
         232 ATEYLQLMVYVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISI 291
Qу
             161 AVSY-QTKVNIL-SAIKSPCHRETLEGAEAKPW-----YEPIYQGGVFQLEKGDRLSA 211
Db
         292 EVSNPSLLD-PDQDATYFG 309
Qу
             |:: | || : || ||
         212 EINLPEYLDYAESGQVYFG 230
Db
RESULT 9
OWHUN
tumor necrosis factor alpha precursor [validated] - human
N; Alternate names: cachectin; TNFA
C; Species: Homo sapiens (man)
C;Date: 28-Aug-1985 #sequence revision 28-Aug-1985 #text change 08-Dec-2000
C; Accession: A93585; S36153; A93351; A44189; B61478; I53311; S62610; I54522;
A01646; B23784
R; Nedwin, G.E.; Naylor, S.L.; Sakaguchi, A.Y.; Smith, D.; Jarrett-Nedwin, J.;
Pennica, D.; Goeddel, D.V.; Gray, P.W.
Nucleic Acids Res. 13, 6361-6373, 1985
A; Title: Human lymphotoxin and tumor necrosis factor genes: structure, homology
and chromosomal localization.
A; Reference number: A93585; MUID: 86016093; PMID: 2995927
A; Accession: A93585
A; Molecule type: DNA
A; Residues: 1-233 <NED>
A; Cross-references: GB: X02910; GB: X02159; NID: q37209; PIDN: CAA26669.1;
PID:q37210
R; Iris, F.J.M.; Bouqueleret, L.; Prieur, S.; Caterina, D.; Primas, G.; Perrot,
V.; Jurka, J.; Rodriguez-Tome, P.; Claverie, J.M.; Dausset, J.; Cohen, D.
Nature Genet. 3, 137-145, 1993
A; Title: Dense Alu clustering and a potential new member of the NFkappaB family
within a 90 kilobase HLA class III segment.
A; Reference number: S36152; MUID: 93272029; PMID: 8499947
A; Accession: S36153
A; Status: nucleic acid sequence not shown; translation not shown
A; Molecule type: DNA
A; Residues: 1-233 <IRI>
A; Cross-references: EMBL: Z15026; NID: g37211; PIDN: CAA78745.1; PID: g37212
A; Note: the nucleotide sequence was submitted to the EMBL Data Library, August
1992
```

F;82/Binding site: carbohydrate (Ser) (covalent) #status predicted

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R; Pennica, D.; Nedwin, G.E.; Hayflick, J.S.; Seeburg, P.H.; Derynck, R.;
Palladino, M.A.; Kohr, W.J.; Aggarwal, B.B.; Goeddel, D.V.
Nature 312, 724-729, 1984
A; Title: Human tumour necrosis factor: precursor structure, expression and
homology to lymphotoxin.
A; Reference number: A93351; MUID: 85086244; PMID: 6392892
A; Accession: A93351
A; Molecule type: mRNA
A; Residues: 1-233 < PEN>
A; Cross-references: GB: X02910; GB: X02159; NID: q37209; PIDN: CAA26669.1;
PID:q37210
A; Note: this protein was isolated from the monocyte-like cell line HL-60 from a
promyelocytic leukemia
R; Wang, A.M.; Creasey, A.A.; Ladner, M.B.; Lin, L.S.; Strickler, J.; Van
Arsdell, J.N.; Yamamoto, R.; Mark, D.F.
Science 228, 149-154, 1985
A; Title: Molecular cloning of the complementary DNA for human tumor necrosis
factor.
A; Reference number: A44189; MUID: 85142190; PMID: 3856324
A; Accession: A44189
A; Molecule type: mRNA
A; Residues: 1-62, 'S', 64-233 <WAN>
A;Cross-references: GB:M10988; NID:g339737; PIDN:AAA61198.1; PID:g339738
R; Fukuda, S.; Ando, S.; Sanou, O.; Taniai, M.; Fujii, M.; Masaki, N.; Nakamura,
K.I.; Ando, O.; Torigoe, K.; Sugimoto, T.; Kurimoto, M.
Lymphokine Res. 7, 175-185, 1988
A; Title: Simultaneous production of natural human tumor necrosis factor-alpha, -
beta and interferon-alpha from BALL-1 cells stimulated by HVJ.
A; Reference number: A61478; MUID: 88301617; PMID: 2841543
A; Accession: B61478
A; Molecule type: protein
A; Residues: 83-102; 109-119; 121-128, 'X', 130-131; 142-144, 'X', 146, 'XXX', 150-
152;159-174;180,'X',182-204 <FUK>
R; Marmenout, A.; Fransen, L.; Tavernier, J.; Van Der Heyden, J.; Tizard, R.;
Kawashima, E.; Shaw, A.; Johnson, M.
Eur. J. Biochem. 152, 515-522, 1985
A; Title: Molecular cloning and expression of human tumor necrosis factor and
comparison with mouse tumor nectosis factor.
A; Reference number: I53311; MUID: 86030296; PMID: 3932069
A; Accession: I53311
A; Status: translated from GB/EMBL/DDBJ
A; Molecule type: DNA
A; Residues: 1-233 <MAR>
A;Cross-references: GB:M26331; NID:g339763; PIDN:AAA36758.1; PID:g339764
A; Experimental source: U-937 cells
R; Takakura-Yamamoto, R.; Yamamoto, S.; Fukuda, S.; Kurimoto, M.
Eur. J. Biochem. 235, 431-437, 1996
A; Title: O-Glycosylated species of natural human tumor-necrosis factor-alpha.
A; Reference number: S62610; MUID: 96202967; PMID: 8631363
A; Accession: S62610
A; Molecule type: protein
A; Residues: 77-99 <TAK>
R; D'Alfonso, S.; Richiardi, P.M.
Immunogenetics 39, 150-154, 1994
A; Title: A polymorphic variation in a putative regulation box of the TNFA
promoter region.
A; Reference number: I54522; MUID: 94102809; PMID: 7903959
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A; Status: preliminary; translated from GB/EMBL/DDBJ
A; Molecule type: DNA
A; Residues: 1-8 < DAL>
A; Cross-references: GB:S68530; NID:g544751
R; Stevenson, F.T.; Bursten, S.L.; Locksley, R.M.; Lovett, D.H.
J. Exp. Med. 176, 1053-1062, 1992
A; Title: Myristyl acylation of the tumor necrosis factor alpha precursor on
specific lysine residues.
A; Reference number: A59163; MUID: 93018820; PMID: 1402651
A; Contents: annotation; identification of myristylated lysines
R; Aggarwal, B.B.; Kohr, W.J.; Hass, P.E.; Moffat, B.; Spencer, S.A.; Henzel,
W.J.; Bringman, T.S.; Nedwin, G.E.; Goeddel, D.V.; Harkins, R.N.
J. Biol. Chem. 260, 2345-2354, 1985
A; Title: Human tumor necrosis factor. Production, purification, and
characterization.
A; Reference number: A92511; MUID: 85130974; PMID: 3871770
A; Contents: annotation; disulfide bond
C; Comment: Secreted from mitogen-activated macrophages within 4-24 hours after
induction, TNF-alpha can cause cytolysis of certain tumor cell lines and have an
antiproliferative effect on others without detriment to normal cells. It can
also act synergistically with interferon gamma to kill certain transformed cell
C; Comment: TNF-alpha and -beta (lymphotoxin) are the products of different genes
closely linked on chromosome 6. They are induced by similar mitogenic stimuli
and have similar biological activities but are produced by different cell types
and have different induction kinetics.
C; Genetics:
A; Gene: GDB: TNF; TNFA
A; Cross-references: GDB:120441; OMIM:191160
A; Map position: 6p21.3-6p21.3
A; Introns: 62/3; 78/1; 94/1
C; Complex: homotrimer
C; Superfamily: tumor necrosis factor
C; Keywords: cytokine; cytotoxin; glycoprotein; homotrimer; lipoprotein;
lymphokine; macrophage; membrane protein; myristylation
F;1-76/Domain: propeptide #status predicted <PRO>
F;77-233/Product: tumor necrosis factor #status experimental <MAT>
F;19,20/Binding site: myristate (Lys) (covalent) #status experimental
F;81/Binding site: carbohydrate (Ser) (covalent) (partial) #status experimental
F;145-177/Disulfide bonds: #status experimental
                          7.9%; Score 133; DB 1; Length 233;
  Query Match
  Best Local Similarity 25.5%; Pred. No. 0.00086;
          40; Conservative 31; Mismatches
                                                62; Indels 24; Gaps
                                                                            8;
          163 QPFAHLTINATDIPSGSHKVSLSSWYHDRGWAKISN-MTFSNGKLIVNQDGFYYLYANIC 221
Qу
             Db
           87 KPVAHVVAN----POAEGOL---OWLNRRANALLANGVELRDNOLVVPSEGLYLIYSQVL 139
          222 FRHH--ETSGDLATEYLQLMV--YVTK----TSIKIPSSHTLMKGGSTKYWSGNSEFHFY 273
QУ
                   :: | | : : | | | :: | |
                                                       : | | | |
         140 FKGQGCPSTHVLLTHTISRIAVSYQTKVNLLSAIKSPCQRETPEGAEAKPW-----YE 192
Db
          274 SINVGGFFKLRSGEEISIEVSNPSLLD-PDQDATYFG 309
Qу
              | :|| |:| |: :| |: : | || :
Db
          193 PIYLGGVFQLEKGDRLSAEINRPDYLDFAESGQVYFG 229
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A; Accession: I54522

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RESULT 10
I54490
tumor necrosis factor alpha precursor - white-footed mouse
C; Species: Peromyscus leucopus (white-footed mouse)
C;Date: 02-Aug-1996 #sequence revision 02-Aug-1996 #text change 04-Feb-2000
C; Accession: I54490
R; Crew, M.D.; Filipowsky, M.E.
Immunogenetics 35, 351-353, 1992
A; Title: Sequence of the tumor necrosis factor/cachectin (TNF) gene from
Peromyscus leucopus (family Cricetidae).
A; Reference number: I54490; MUID: 92218012; PMID: 1348497
A:Accession: I54490
A; Status: preliminary; translated from GB/EMBL/DDBJ
A; Molecule type: DNA
A; Residues: 1-235 < RES>
A;Cross-references: GB:M59233; NID:q202506; PIDN:AAA40596.1; PID:q202507
C; Genetics:
A; Gene: PlTNF
A; Introns: 62/3; 81/1; 97/1
C; Superfamily: tumor necrosis factor
C; Keywords: glycoprotein; lipoprotein; myristylation
F;19,20/Binding site: myristate (Lys) (covalent) #status predicted
F;84/Binding site: carbohydrate (Ser) (covalent) #status predicted
                           7.9%; Score 132.5; DB 2; Length 235;
  Query Match
                         25.3%; Pred. No. 0.00096;
  Best Local Similarity
           42; Conservative 27; Mismatches 54; Indels 43; Gaps
  Matches
          163 QPFAHLTINATDIPSGSHKVSLSSWYHDRGWAKISNMTFSNG-----KLIVNQDGFYYL 216
QУ
                                                             :|:: || |:
                              |:| :| :| :|
           90 KPVAHVVAN-----HQVDEQLEWLSRG---ANALLANGMDLKDNQLVIPADGLYLV 137
Db
          217 YANICFRHHETSGDLATEYLQLMVYVTK-----TSIKIPSSHTLMKGGSTKYW 264
QУ
                       | : |: | ::
                                                     ::|| |
          138 YSQVLFK-----GQGCSSYVLLTHTVSRFAVSYEDKVNLLSAIKSPCPKETPEGSELKPW 192
Db
         265 SGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD-PDQDATYFG 309
Qу
                    : | : | | | : | | | : | | | | : |
Db
          193 -----YEPIYLGGVFQLEKGDRLSAEVNLPKYLDFAESGQVYFG 231
RESULT 11
JU0029
tumor necrosis factor alpha precursor - rat
N; Alternate names: cachectin; TNF alpha
C; Species: Rattus norvegicus (Norway rat)
C;Date: 07-Jun-1990 #sequence revision 07-Jun-1990 #text change 04-Feb-2000
C; Accession: JU0029; JN0868; S21674
R; Shirai, T.; Shimizu, N.; Horiguchi, S.; Ito, H.
Agric. Biol. Chem. 53, 1733-1736, 1989
A; Title: Cloning and expression in Escherichia coli of the gene for rat tumor
necrosis factor.
A; Reference number: JU0029
A; Accession: JU0029
A; Molecule type: DNA
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A; Residues: 1-235 <SHI>
R; Kwon, J.; Chung, I.Y.; Benveniste, E.N.
Gene 132, 227-236, 1993
A; Title: Cloning and sequence analysis of the rat tumor necrosis factor-encoding
genes.
A; Reference number: JN0868; MUID: 94040766; PMID: 8224868
A; Accession: JN0868
A; Molecule type: DNA
A; Residues: 1-235 <KWO>
A;Cross-references: GB:L00981; NID:g205253; PIDN:AAA16275.1; PID:g205254
R; Estler, H.C.; Grewe, M.; Gaussling, R.; Pavlovic, M.; Decker, K.
Biol. Chem. Hoppe-Seyler 373, 271-281, 1992
A; Title: Rat tumor necrosis factor-alpha. Transcription in rat Kupffer cells and
in vitro posttranslational processing based on a PCR-derived cDNA.
A; Reference number: S21674; MUID: 92329007; PMID: 1627266
A; Accession: S21674
A; Molecule type: mRNA
A; Residues: 1-38, 'P', 40-162, 'T', 164-201, 'S', 203-235 <EST>
A; Cross-references: GB: X66539; GB: S40199; NID: g395369; PIDN: CAA47146.1;
PID:g395370
C; Comment: Tumor necrosis factor is secreted by macrophages in response to
endotoxin and produces hemorrhagic necrosis of tumors.
C; Genetics:
A; Gene: TNF-alpha
A; Introns: 62/3; 81/1; 97/1
C; Superfamily: tumor necrosis factor
C; Keywords: cytokine; cytotoxin; glycoprotein; lipoprotein; lymphokine;
macrophage; membrane protein; myristylation
F;80-235/Product: tumor necrosis factor #status predicted <MAT>
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F;84/Binding site: carbohydrate (Ser) (covalent) #status predicted
F;86/Binding site: carbohydrate (Asn) (covalent) #status predicted
F;148-179/Disulfide bonds: #status predicted
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         163 QPFAHLTINATDIPSGSHKVSLS-SWYHDRGWAKISN-MTFSNGKLIVNQDGFYYLYANI 220
Qу
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                                    90 KPVAHVVAN------HQAEEQLEWLSQRANALLANGMDLKDNQLVVPADGLYLIYSQV 141
Db
         221 CFRHHETSGDLATEYLQLMVYVTK-----TSIKIPSSHTLMKGGSTKYWSGNS 268
QУ
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                                                                1 1
              |:
         142 LFK-----GQGCPDYVLLTHTVSRFAISYQEKVSLLSAIKSPCPKDTPEGAELKPW---- 192
Db
         269 EFHFYSINVGGFFKLRSGEEISIEVSNPSLLD-PDQDATYFG 309
Qу
                : ::|| |:| |: | ||: | || || : | |||
         193 ---YEPMYLGGVFQLEKGDLLSAEVNLPKYLDITESGQVYFG 231
Db
RESULT 12
I49139
lymphotoxin-beta - mouse
C; Species: Mus musculus (house mouse)
C;Date: 02-Jul-1996 #sequence revision 02-Jul-1996 #text change 05-Nov-1999
C; Accession: I49139; I49138; I49076
```

```
R; Lawton, P.; Nelson, J.; Tizard, R.; Browning, J.L.
J. Immunol. 154, 239-246, 1995
A; Title: Characterization of the mouse lymphotoxin-beta gene.
A; Reference number: I49138; MUID: 95088371; PMID: 7995944
A; Accession: I49139
A; Status: translated from GB/EMBL/DDBJ
A; Molecule type: mRNA
A; Residues: 1-306 < RES>
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A; Accession: I49138
A; Status: translated from GB/EMBL/DDBJ
A; Molecule type: DNA
A; Residues: 1-306 < RE3>
A; Cross-references: EMBL: U16984; NID: q577431; PIDN: AAB60493.1; PID: q577432
R; Pokholok, D.K.; Maroulakou, I.G.; Kuprash, D.V.; Alimzhanov, M.B.; Kozlov,
S.V.; Novobrantseva, T.I.; Turetskaya, R.L.; Green, J.E.; Nedospasov, S.A.
Proc. Natl. Acad. Sci. U.S.A. 92, 674-678, 1995
A; Title: Cloning and expression analysis of the murine lymphotoxin beta gene.
A; Reference number: A55602; MUID: 95148600; PMID: 7846035
A; Accession: I49076
A; Status: preliminary
A; Molecule type: DNA
A; Residues: 1-306 < RE2>
A;Cross-references: EMBL:U12029; NID:g515508; PIDN:AAA67716.1; PID:g515509
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A; Gene: LT-beta
A; Introns: 54/3; 160/1
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Qу
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Db
                  162 AQPFAHLTIN--ATDIPSGSHKVSLS-----SWYHDRG--WAKISNMTF----- 201
QУ
                              ] | | : : : : : : :
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                  125 LSPAADSTPDPGVQQLPKGEPETDLNPELPAAHLIGAWMSGQGLSWEASQEEAFLRSGAQ 184
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Qу
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Db
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Qy
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RESULT 13
S22052
tumor necrosis factor alpha precursor - baboon
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C; Species: Papio sp. (baboon)

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C;Date: 10-Sep-1999 #sequence revision 10-Sep-1999 #text_change 04-Feb-2000
C; Accession: S22052
R; Sanjanwala, M.; Edwards, A.
submitted to the EMBL Data Library, September 1991
A; Description: Baboon Tumor Necrosis Factor Derived from Sequences of Genomic
DNA.
A; Reference number: S22052
A; Accession: S22052
A; Status: preliminary
A; Molecule type: DNA
A; Residues: 1-233 <SAN>
A; Cross-references: EMBL: X62141; NID: g38159; PIDN: CAA44068.1; PID: g38160
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A; Introns: 62/3; 78/1; 94/1
C; Superfamily: tumor necrosis factor
C; Keywords: glycoprotein; lipoprotein; myristylation; transmembrane protein
F;19,20/Binding site: myristate (Lys) (covalent) #status predicted
F;81/Binding site: carbohydrate (Ser) (covalent) #status predicted
F;145-177/Disulfide bonds: #status predicted
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          222 FRHH--ETSGDLATEYLOLMV--YVTK----TSIKIPSSHTLMKGGSTKYWSGNSEFHFY 273
QУ
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         140 FKGQGCPSTHVLLTHTISRIAVSYQTKVNLLSAIKSPCQRETPEGAEAKPW-----YE 192
Db
         274 SINVGGFFKLRSGEEISIEVSNPSLLD-PDQDATYFG 309
Qу
               | :|| |:| |: :| |:: | || :
Db
          193 PIYLGGVFQLEKGDRLSAEINLPDYLDFAESGQVYFG 229
RESULT 14
JQ1344
tumor necrosis factor alpha precursor - horse
N; Alternate names: cachectin; TNF alpha
C; Species: Equus caballus (domestic horse)
C;Date: 10-Sep-1999 #sequence revision 10-Sep-1999 #text_change 04-Feb-2000
C; Accession: JQ1344
R; Su, X.; Morris, D.D.; McGraw, R.A.
Gene 107, 319-321, 1991
A; Title: Cloning and characterization of gene TNF alpha encoding equine tumor
necrosis factor alpha.
A; Reference number: JQ1344; MUID: 92084125; PMID: 1748301
A; Accession: JQ1344
A; Molecule type: DNA
A; Residues: 1-234 <SUX>
A;Cross-references: GB:M64087; NID:g164244; PIDN:AAA30959.1; PID:g164245
C; Comment: This protein is an important proximal mediator of endotoxemia.
C; Genetics:
A; Gene: TNF-alpha
A; Introns: 62/3; 79/1; 95/1
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C; Superfamily: tumor necrosis factor
C; Keywords: cytokine; cytotoxin; glycoprotein; lipoprotein; lymphokine;
macrophage; membrane protein; myristylation
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F;82/Binding site: carbohydrate (Ser) (covalent) #status predicted
F;146-178/Disulfide bonds: #status predicted
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Db
         222 FRHHETSGDLATEYLQLMVYVTKTSIKIPSSHTLMKG-----GSTKYWSGNSE 269
Qу
             |: | :| | | ::::: || |:
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Db
         270 FHFYSINVGGFFKLRSGEEISIEVSNPSLLD-PDQDATYFG 309
Qу
              192 --YEPIYLGGVFQLEKGDQLSAEINQPNYLDFAESGQVYFG 230
Db
RESULT 15
S24642
tumor necrosis factor alpha precursor - bovine
C; Species: Bos primigenius taurus (cattle)
C;Date: 10-Sep-1999 #sequence revision 10-Sep-1999 #text change 04-Feb-2000
C; Accession: I46047; S24642
R; Cludts, I.; Cleuter, Y.; Kettmann, R.; Burny, A.; Droogmans, L.
Cytokine 5, 336-341, 1993
A; Title: Cloning and characterization of the tandemly arranged bovine
lymphotoxin and tumour necrosis factor-alpha genes.
A; Reference number: I46046; MUID: 94083525; PMID: 8260599
A; Accession: I46047
A; Status: preliminary; translated from GB/EMBL/DDBJ
A; Molecule type: DNA
A; Residues: 1-233 <CL2>
A;Cross-references: EMBL:Z14137; NID:g796; PIDN:CAA78511.1; PID:g798
C; Genetics:
A; Gene: TNFA
A; Introns: 62/3; 78/1; 94/1
C; Superfamily: tumor necrosis factor
C; Keywords: glycoprotein; lipoprotein; myristylation; transmembrane protein
F;20/Binding site: myristate (Lys) (covalent) #status predicted
F;81/Binding site: carbohydrate (Ser) (covalent) #status predicted
F;145-177/Disulfide bonds: #status predicted
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          55 VIGPQREESPGGPSINSPLVQTLRSSSQASSNKPVAHV---VADINSPGQL----- 102
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Search completed: February 25, 2004, 16:31:07 Job time : 31 secs

GenCore version 5.1.6 Copyright (c) 1993 - 2004 Compugen Ltd.

OM protein - protein search, using sw model

Run on: February 25, 2004, 16:30:32; Search time 36 Seconds

(without alignments)

1859.322 Million cell updates/sec

Title: US-09-787-126-2

Perfect score: 1685

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Scoring table: BLOSUM62

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Searched: 809742 segs, 211153259 residues

Total number of hits satisfying chosen parameters: 809742

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%

Maximum Match 100%

Listing first 45 summaries

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18: /cgn2 6/ptodata/1/pubpaa/US60 PUBCOMB.pep:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

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Result Query

> Score Match Length DB ID No.

Description

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3	1685	100.0	317	9	US-09-877-650-13	Sequence 13, Appl
4	1685	100.0	317	14	US-10-218-547-22	Sequence 22, Appl
5	1685	100.0	317	14	US-10-405-878-13	Sequence 13, Appl
6	1685	100.0	317	14	US-10-167-182-11	Sequence 11, Appl
7	1685	100.0	317	14	US-10-310-793-28	Sequence 28, Appl
8	1685	100.0	317	15	US-10-460-623-11	Sequence 11, Appl
9	1417.5	84.1	316	10	US-09-079-569-7	Sequence 7, Appli
10	1417.5	84.1	316	10	US-09-873-829-4	Sequence 4, Appli
11	1417.5	84.1	316	13	US-10-017-910-4	Sequence 4, Appli
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13	1417.5	84.1	316	14	US-10-272-411-19	Sequence 19, Appl
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24	1301	77.2	246	14	US-10-167-182-17	Sequence 17, Appl
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35	1109	65.8	244	14	US-10-167-182 - 16	Sequence 16, Appl
36	1109	65.8	244	15	US-10-460-623-16	Sequence 16, Appl
37	962	57.1	185	14	US-10-050-902-320	Sequence 320, App
38	962	57.1	185	14	US-10-050-898-320	Sequence 320, App
39	909	53.9	199	14	US-10-050-902-224	Sequence 224, App
40	909	53.9	199	14	US-10-050-898-224	Sequence 224, App
41	852	50.6	160	9	US-09-779-050A-15	Sequence 15, Appl
42	848	50.3	178	15	US-10-338-785A-2	Sequence 2, Appli
43	825	49.0	419	14	US-10-050-902-318	Sequence 318, App
44	825	49.0	419	14	US-10-050-898-318	Sequence 318, App
45	809	48.0	151	14	US-10-338-083-10	Sequence 10, Appl

ALIGNMENTS

RESULT 1

US-09-813-329-7

- ; Sequence 7, Application US/09813329
 ; Patent No. US20020012968A1
- ; GENERAL INFORMATION:
- ; APPLICANT: Bristol-Myers Suibb Company

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; TITLE OF INVENTION: No. US20020012968A1el Drosophila Tumor Necrosis Factor
Class Molecule ("DmTNF") and
  TITLE OF INVENTION: Variants Thereof
  FILE REFERENCE: D0016.np
  CURRENT APPLICATION NUMBER: US/09/813,329
  CURRENT FILING DATE: 2001-03-20
  PRIOR APPLICATION NUMBER: 60/190,816
  PRIOR FILING DATE: 2000-03-21
; NUMBER OF SEQ ID NOS: 65
  SOFTWARE: PatentIn version 3.0
; SEQ ID NO 7
   LENGTH: 317
   TYPE: PRT
   ORGANISM: Drosophila melanogaster
US-09-813-329-7
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RESULT 2
US-09-871-856-13
; Sequence 13, Application US/09871856
; Patent No. US20020081720A1
   GENERAL INFORMATION:
       APPLICANT: Anderson, Dirk M.
                 Galibert, Laurent
                 Maraskovsky, Eugene
       TITLE OF INVENTION: Receptor Activator of NF-kappaB
       NUMBER OF SEQUENCES: 19
        CORRESPONDENCE ADDRESS:
            ADDRESSEE: Immunex Corporation, Law Department
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STREET: 51 University Street
            CITY: Seattle
            STATE: WA
            COUNTRY: USA
            ZIP: 98101
       COMPUTER READABLE FORM:
           MEDIUM TYPE: Floppy disk
            COMPUTER: Apple Power Macintosh
            OPERATING SYSTEM: Apple Operating System 7.5.5
            SOFTWARE: Microsoft Word for Power Macintosh 6.0.1
       CURRENT APPLICATION DATA:
            APPLICATION NUMBER: US/09/871,856
            FILING DATE: 31-May-2001
            CLASSIFICATION: <Unknown>
       PRIOR APPLICATION DATA:
           APPLICATION NUMBER: 08/996,139
            FILING DATE: <Unknown>
            APPLICATION NUMBER: USSN 08/813,509
            FILING DATE: 07 MARCH 1997
            APPLICATION NUMBER: USSN 08/772,330
            FILING DATE: 23 DECEMBER 1996
       ATTORNEY/AGENT INFORMATION:
            NAME: Perkins, Patricia Anne
            REGISTRATION NUMBER: 34,693
            REFERENCE/DOCKET NUMBER: 2851-A
       TELECOMMUNICATION INFORMATION:
            TELEPHONE: (206) 587-0430
            TELEFAX: (206)233-0644
   INFORMATION FOR SEQ ID NO: 13:
       SEQUENCE CHARACTERISTICS:
            LENGTH: 317 amino acids
            TYPE: amino acid
            TOPOLOGY: linear
       MOLECULE TYPE: protein
       SEQUENCE DESCRIPTION: SEQ ID NO: 13:
US-09-871-856-13
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; Sequence 13, Application US/09877650
; Patent No. US20020169117A1
   GENERAL INFORMATION:
        APPLICANT: Anderson, Dirk M.
                   Galibert, Laurent
;
                   Maraskovsky, Eugene
        TITLE OF INVENTION: Ligand for Receptor Activator of NF-kappaB
        NUMBER OF SEQUENCES: 19
        CORRESPONDENCE ADDRESS:
             ADDRESSEE: Immunex Corporation, Law Department
             STREET: 51 University Street
             CITY: Seattle
             STATE: WA
             COUNTRY: USA
             ZIP: 98101
        COMPUTER READABLE FORM:
             MEDIUM TYPE: Floppy disk
             COMPUTER: Apple Power Macintosh
             OPERATING SYSTEM: Apple Operating System 7.5.5
             SOFTWARE: Microsoft Word for Power Macintosh 6.0.1
        CURRENT APPLICATION DATA:
             APPLICATION NUMBER: US/09/877,650
             FILING DATE: 08-Jun-2001
             CLASSIFICATION: <Unknown>
        PRIOR APPLICATION DATA:
             APPLICATION NUMBER: 08/995,659
             FILING DATE: 1997-12-22
             APPLICATION NUMBER: USSN 08/813,509
             FILING DATE: 07 MARCH 1997
             APPLICATION NUMBER: USSN 08/772,330
             FILING DATE: 23 DECEMBER 1996
       ATTORNEY/AGENT INFORMATION:
             NAME: Perkins, Patricia Anne
             REGISTRATION NUMBER: 34,693
             REFERENCE/DOCKET NUMBER: 2852-A
        TELECOMMUNICATION INFORMATION:
             TELEPHONE: (206) 587-0430
             TELEFAX: (206)233-0644
   INFORMATION FOR SEQ ID NO: 13:
        SEQUENCE CHARACTERISTICS:
             LENGTH: 317 amino acids
             TYPE: amino acid
             TOPOLOGY: linear
        MOLECULE TYPE: protein
        SEQUENCE DESCRIPTION: SEQ ID NO: 13:
US-09-877-650-13
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US-10-218-547-22
: Sequence 22, Application US/10218547
: Publication No. US20030100074A1
; GENERAL INFORMATION:
  APPLICANT: Human Genome Sciences, Inc.
  TITLE OF INVENTION: Methods And Compositions For Treating Metabolic Bone
Diseases Relating To
  TITLE OF INVENTION: Human Endokine Alpha
  FILE REFERENCE: PF561
  CURRENT APPLICATION NUMBER: US/10/218,547
  CURRENT FILING DATE: 2002-08-15
  PRIOR APPLICATION NUMBER: 60/312,542
  PRIOR FILING DATE: 2001-08-16
  PRIOR APPLICATION NUMBER: 60/330,761
  PRIOR FILING DATE: 2001-10-30
  NUMBER OF SEQ ID NOS: 57
  SOFTWARE: PatentIn version 3.1
; SEQ ID NO 22
   LENGTH: 317
   TYPE: PRT
   ORGANISM: human
US-10-218-547-22
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; Sequence 13, Application US/10405878
; Publication No. US20030175840A1
   GENERAL INFORMATION:
       APPLICANT: Anderson, Dirk M.
                 Galibert, Laurent
                 Maraskovsky, Eugene
       TITLE OF INVENTION: Receptor Activator of NF-kappaB
       NUMBER OF SEQUENCES: 19
       CORRESPONDENCE ADDRESS:
            ADDRESSEE: Immunex Corporation, Law Department
            STREET: 51 University Street
            CITY: Seattle
            STATE: WA
            COUNTRY: USA
            ZIP: 98101
       COMPUTER READABLE FORM:
            MEDIUM TYPE: Floppy disk
            COMPUTER: Apple Power Macintosh
            OPERATING SYSTEM: Apple Operating System 7.5.5
            SOFTWARE: Microsoft Word for Power Macintosh 6.0.1
        CURRENT APPLICATION DATA:
            APPLICATION NUMBER: US/10/405,878
            FILING DATE: 01-Apr-2003
            CLASSIFICATION: <Unknown>
       PRIOR APPLICATION DATA:
            APPLICATION NUMBER: US/08/996,139
            FILING DATE: 22 DECEMBER 1997
            APPLICATION NUMBER: USSN 60/064,671
            FILING DATE: 14 OCTOBER 1997
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APPLICATION NUMBER: USSN 08/813,509
           FILING DATE: 07 MARCH 1997
;
           APPLICATION NUMBER: USSN 08/772,330
           FILING DATE: 23 DECEMBER 1996
       ATTORNEY/AGENT INFORMATION:
           NAME: Perkins, Patricia Anne
           REGISTRATION NUMBER: 34,693
           REFERENCE/DOCKET NUMBER: 2851-A
       TELECOMMUNICATION INFORMATION:
           TELEPHONE: (206) 587-0430
           TELEFAX: (206)233-0644
;
   INFORMATION FOR SEQ ID NO: 13:
       SEQUENCE CHARACTERISTICS:
           LENGTH: 317 amino acids
           TYPE: amino acid
           TOPOLOGY: linear
       MOLECULE TYPE: protein
       SEQUENCE DESCRIPTION: SEQ ID NO: 13:
US-10-405-878-13
                      100.0%; Score 1685; DB 14; Length 317;
 Query Match
                    100.0%; Pred. No. 9.4e-156;
 Best Local Similarity
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RESULT 6
US-10-167-182-11
; Sequence 11, Application US/10167182
; Publication No. US20030176647A1
; GENERAL INFORMATION:
  APPLICANT: Yamaguchi, Kyoji
  APPLICANT: Yasuda, Hisataka
; APPLICANT: Nakagawa, No. US20030176647Aluaki
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APPLICANT: Shima, No. US20030176647Aluyuki
  APPLICANT: Kinosaki, Masahiko
  APPLICANT: Tsuda, Eisuke
  APPLICANT: Goto, Masaaki
  APPLICANT: Yano, Kazuki
            Tomoyasu, Akihiro
  APPLICANT:
            Kobayashi, Fumie
  APPLICANT:
  APPLICANT: Washida, Naohiro
  APPLICANT: Takahashi, Ken
  APPLICANT: Morinaga, Tomonori
  APPLICANT: Higashio, Kanji
  TITLE OF INVENTION: Antibodies to OCIF-binding Molecules
  FILE REFERENCE: FJN-070DV
  CURRENT APPLICATION NUMBER: US/10/167,182
  CURRENT FILING DATE: 2002-06-11
  PRIOR APPLICATION NUMBER: US 09/202,455
  PRIOR FILING DATE: 1998-12-15
  PRIOR APPLICATION NUMBER: JP 97808/1997
  PRIOR FILING DATE: 1997-04-15
  PRIOR APPLICATION NUMBER: JP 151434/1997
  PRIOR FILING DATE: 1997-06-09
  PRIOR APPLICATION NUMBER: JP 217897/1997
  PRIOR FILING DATE: 1997-08-12
  PRIOR APPLICATION NUMBER: JP 224803/1997
  PRIOR FILING DATE: 1997-08-21
  PRIOR APPLICATION NUMBER: JP 332241/1997
  PRIOR FILING DATE: 1997-12-02
  PRIOR APPLICATION NUMBER: WO PCT/JP98/01728
  PRIOR FILING DATE: 1998-04-15
  NUMBER OF SEQ ID NOS: 19
  SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 11
   LENGTH: 317
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   ORGANISM: Homo sapiens
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RESULT 7
US-10-310-793-28
; Sequence 28, Application US/10310793
: Publication No. US20030198640A1
; GENERAL INFORMATION:
; APPLICANT: Yu, Guo-Liang
; APPLICANT: Ni, Jian
; APPLICANT: Rosen, Craig A
; APPLICANT: Zhang, Jun
  APPLICANT: Wei, Ping
  TITLE OF INVENTION: Methods And Compositions For Treating Inflammatory Bowel
  TITLE OF INVENTION: Relating To Human Tumor Necrosis Factor-Gamma Beta
  FILE REFERENCE: PF573
  CURRENT APPLICATION NUMBER: US/10/310,793
  CURRENT FILING DATE: 2002-12-06
; PRIOR APPLICATION NUMBER: 60/336,695
  PRIOR FILING DATE: 2001-12-07
  PRIOR APPLICATION NUMBER: 10/226,294
; PRIOR FILING DATE: 2002-08-23
; PRIOR APPLICATION NUMBER: 60/314,381
; PRIOR FILING DATE: 2001-08-24
; PRIOR APPLICATION NUMBER: 09/899,059
; PRIOR FILING DATE: 2001-07-06
  PRIOR APPLICATION NUMBER: 60/278,449
  PRIOR FILING DATE: 2001-03-26
  PRIOR APPLICATION NUMBER: 60/216,879
  PRIOR FILING DATE: 2000-07-07
  PRIOR APPLICATION NUMBER: 09/559,290
  PRIOR FILING DATE: 2000-04-27
  PRIOR APPLICATION NUMBER: 60/180,908
  PRIOR FILING DATE: 2000-02-08
  PRIOR APPLICATION NUMBER: 60/134,067
  PRIOR FILING DATE: 1999-05-13
  PRIOR APPLICATION NUMBER: 60/132,227
  PRIOR FILING DATE: 1999-05-03
  Remaining Prior Application data removed - See File Wrapper or PALM.
; NUMBER OF SEQ ID NOS: 71
  SOFTWARE: PatentIn version 3.1
; SEQ ID NO 28
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    TYPE: PRT
    ORGANISM: human
US-10-310-793-28
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  Query Match
  Best Local Similarity 100.0%; Pred. No. 9.4e-156;
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; Sequence 11, Application US/10460623
; Publication No. US20030208045A1
; GENERAL INFORMATION:
; APPLICANT: Yamaguchi, Kyoji
; APPLICANT: Yasuda, Hisataka
  APPLICANT: Nakagawa, No. US20030208045Aluaki
  APPLICANT: Shima, No. US20030208045Aluyuki
  APPLICANT: Kinosaki, Masahiko
  APPLICANT: Tsuda, Eisuke
  APPLICANT: Goto, Masaaki
  APPLICANT: Yano, Kazuki
  APPLICANT: Tomoyasu, Akihiro
  APPLICANT: Kobayashi, Fumie
  APPLICANT: Washida, Naohiro
  APPLICANT: Takahashi, Ken
  APPLICANT: Morinaga, Tomonori
  APPLICANT: Higashio, Kanji
  TITLE OF INVENTION: No. US20030208045A1el Protein and Method for Producing
the Protein
 FILE REFERENCE: FJN-070
  CURRENT APPLICATION NUMBER: US/10/460,623
  CURRENT FILING DATE: 2003-06-13
  PRIOR APPLICATION NUMBER: JP 97808/1997
  PRIOR FILING DATE: 1997-04-15
  PRIOR APPLICATION NUMBER: JP 151434/1997
  PRIOR FILING DATE: 1997-06-09
  PRIOR APPLICATION NUMBER: JP 217897/1997
   PRIOR FILING DATE: 1997-08-12
; PRIOR APPLICATION NUMBER: JP 224803/1997
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  PRIOR FILING DATE: 1997-12-02
  PRIOR APPLICATION NUMBER: WO PCT/JP98/01728
  PRIOR FILING DATE: 1998-04-15
  NUMBER OF SEQ ID NOS: 19
  SOFTWARE: PatentIn Ver. 2.0
 SEQ ID NO 11
   LENGTH: 317
   TYPE: PRT
   ORGANISM: Homo sapiens
US-10-460-623-11
                     100.0%; Score 1685; DB 15; Length 317;
 Query Match
                     100.0%; Pred. No. 9.4e-156;
 Best Local Similarity
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 Matches 317; Conservative 0; Mismatches
                                         0; Indels
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            301 PDQDATYFGAFKVRDID 317
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RESULT 9
US-09-079-569-7
; Sequence 7, Application US/09079569
; Publication No. US20030104485A1
  GENERAL INFORMATION:
    APPLICANT: Boyle, William J.
    TITLE OF INVENTION: OSTEOPROTEGERIN BINDING PROTEINS
    NUMBER OF SEQUENCES: 7
    CORRESPONDENCE ADDRESS:
      ADDRESSEE: Amgen Inc.
      STREET: 1840 Dehavilland Drive
      CITY: Thousand Oaks
      STATE: California
      COUNTRY: USA
      ZIP: 91230-1789
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PRIOR FILING DATE: 1997-08-21

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COMPUTER READABLE FORM:
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     OPERATING SYSTEM: PC-DOS/MS-DOS
     SOFTWARE: PatentIn Release #1.0, Version #1.30
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     FILING DATE:
     CLASSIFICATION:
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     APPLICATION NUMBER: 08/842,842
     FILING DATE:
   ATTORNEY/AGENT INFORMATION:
     NAME: Winter, Robert B.
     REFERENCE/DOCKET NUMBER: A-451
  INFORMATION FOR SEQ ID NO: 7:
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     LENGTH: 316 amino acids
     TYPE: amino acid
     TOPOLOGY: linear
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 Query Match
 Best Local Similarity 84.3%; Pred. No. 1.1e-129;
 Matches 268; Conservative 16; Mismatches 31; Indels
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; Sequence 4, Application US/09873829
; Publication No. US20030185820A1
   GENERAL INFORMATION:
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APPLICANT: Choi, Yongwon
                  Wong, Brian
                  Josien, Regis
                  Steinman, Ralph
        TITLE OF INVENTION: A PROTEIN BELONGING TO THE THE SUPERFAMILY
                          INVOLVED IN SIGNAL TRANSDUCTION, NUCLEIC ACIDS
ENCODING SAME, AND
                          METHODS OF USE THEREOF
        NUMBER OF SEQUENCES: 18
;
        CORRESPONDENCE ADDRESS:
            ADDRESSEE: Klauber & Jackson
            STREET: 411 Hackensack Avenue, 4th Floor
            CITY: Hackensack
            STATE: New Jersey
            COUNTRY: USA
            ZIP: 07601
        COMPUTER READABLE FORM:
            MEDIUM TYPE: Floppy disk
            COMPUTER: IBM PC compatible
            OPERATING SYSTEM: PC-DOS/MS-DOS
            SOFTWARE: PatentIn Release #1.0, Version #1.30
       CURRENT APPLICATION DATA:
            APPLICATION NUMBER: US/09/873,829
            FILING DATE: 04-Jun-2001
            CLASSIFICATION: <Unknown>
       PRIOR APPLICATION DATA:
            APPLICATION NUMBER: 09/210,115
            FILING DATE: <Unknown>
        ATTORNEY/AGENT INFORMATION:
            NAME: Jackson Esq., David A.
            REGISTRATION NUMBER: 26,742
             REFERENCE/DOCKET NUMBER: 600-1-200 CIP N
        TELECOMMUNICATION INFORMATION:
             TELEPHONE: 201-487-5800
             TELEFAX: 201-343-1684
             TELEX: 133521
   INFORMATION FOR SEQ ID NO: 4:
        SEQUENCE CHARACTERISTICS:
            LENGTH: 316 amino acids
             TYPE: amino acid
             TOPOLOGY: linear
        MOLECULE TYPE: protein
        SEQUENCE DESCRIPTION: SEQ ID NO: 4:
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; Publication No. US20020159970A1
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        APPLICANT: Choi, Yongwon
                  Wong, Brian
;
                  Josien, Regis
                  Steinman, Ralph
        TITLE OF INVENTION: A PROTEIN BELONGING TO THE THE SUPERFAMILY
                          INVOLVED IN SIGNAL TRANSDUCTION, NUCLEIC ACIDS
ENCODING SAME, AND
                          METHODS OF USE THEREOF
        NUMBER OF SEQUENCES: 14
        CORRESPONDENCE ADDRESS:
            ADDRESSEE: Klauber & Jackson
            STREET: 411 Hackensack Avenue, 4th Floor
            CITY: Hackensack
            STATE: New Jersey
            COUNTRY: USA
            ZIP: 07601
        COMPUTER READABLE FORM:
            MEDIUM TYPE: Floppy disk
            COMPUTER: IBM PC compatible
            OPERATING SYSTEM: PC-DOS/MS-DOS
            SOFTWARE: PatentIn Release #1.0, Version #1.30
        CURRENT APPLICATION DATA:
            APPLICATION NUMBER: US/10/017,910
            FILING DATE: 14-Dec-2001
            CLASSIFICATION: <Unknown>
        PRIOR APPLICATION DATA:
            APPLICATION NUMBER: US 09/447,035
             FILING DATE: 1999-11-22
        ATTORNEY/AGENT INFORMATION:
             NAME: Jackson Esq., David A.
             REGISTRATION NUMBER: 26,742
            REFERENCE/DOCKET NUMBER: 600-1-200
        TELECOMMUNICATION INFORMATION:
             TELEPHONE: 201-487-5800
;
             TELEFAX: 201-343-1684
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            LENGTH: 316 amino acids
            TYPE: amino acid
            TOPOLOGY: linear
       MOLECULE TYPE: protein
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US-10-017-910-4
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; Publication No. US20030013651A1
: GENERAL INFORMATION:
; APPLICANT: Barnes-Jewish Hospital, d/b/a The Jewish Hospital of St. Louis
  TITLE OF INVENTION: STIMULATION OF OSTEOGENESIS USING RANK LIGAND FUSION
  FILE REFERENCE: BJCH 10054.1
  CURRENT APPLICATION NUMBER: US/10/105,057
  CURRENT FILING DATE: 2002-03-22
  PRIOR APPLICATION NUMBER: US 60/277,855
  PRIOR FILING DATE: 2001-03-22
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84.1%; Score 1417.5; DB 14; Length 316;

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US-10-272-411-19
; Sequence 19, Application US/10272411
; Publication No. US20030100068A1
; GENERAL INFORMATION:
; APPLICANT: Barnes Jewish Hospital
; APPLICANT: Lam, Jonathan
; APPLICANT: Ross, F. Patrick
; APPLICANT: Teitelbaum, Steven
; TITLE OF INVENTION: RANKL MIMICS AND USES THEREOF
; FILE REFERENCE: 60019620-0202
; CURRENT APPLICATION NUMBER: US/10/272,411
; CURRENT FILING DATE: 2002-10-15
; PRIOR APPLICATION NUMBER: 60/329,393
; PRIOR FILING DATE: 2001-10-15
; NUMBER OF SEQ ID NOS: 52
; SOFTWARE: PatentIn version 3.1
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; ORGANISM: Homo sapiens
US-10-272-411-19
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Best Local Similarity 84.3%; Pred. No. 1.1e-129;

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; Publication No. US20030109444A1
; GENERAL INFORMATION:
    APPLICANT: Barnes Jewish Hospital
    APPLICANT: Lam, Jonathan
     APPLICANT: Ross, F. Patrick
     APPLICANT: Teitelbaum, Steven
     TITLE OF INVENTION: RANKL MIMICS AND USES THEREOF
     FILE REFERENCE: 60019620-0206
     CURRENT APPLICATION NUMBER: US/10/272,328A
     CURRENT FILING DATE: 2003-01-24
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     PRIOR FILING DATE: 2001-10-15
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; Sequence 2, Application US/10326052
; Publication No. US20030144480A1
   GENERAL INFORMATION:
        APPLICANT: Gorman, Daniel M.
                  Mattson, Jeanine D.
        TITLE OF INVENTION: Mammalian Cell Surface Antigens; Related
                          Reagents
        NUMBER OF SEQUENCES: 2
        CORRESPONDENCE ADDRESS:
             ADDRESSEE: DNAX Research Institute
             STREET: 901 California Avenue
             CITY: Palo Alto
             STATE: California
             COUNTRY: USA
             ZIP: 94304-1104
        COMPUTER READABLE FORM:
             MEDIUM TYPE: Floppy disk
             COMPUTER: IBM PC compatible
             OPERATING SYSTEM: PC-DOS/MS-DOS
             SOFTWARE: PatentIn Release #1.0, Version #1.30
        CURRENT APPLICATION DATA:
             APPLICATION NUMBER: US/10/326,052
             FILING DATE: 23-Dec-2002
             CLASSIFICATION: <Unknown>
        PRIOR APPLICATION DATA:
             APPLICATION NUMBER: US/09/671,658A
             FILING DATE: 27-Sep-2000
             APPLICATION NUMBER: US/08/989,362
             FILING DATE: 12-DEC-1997
             APPLICATION NUMBER: US 60/032,846
             FILING DATE: 13-DEC-1996
        ATTORNEY/AGENT INFORMATION:
             NAME: Ching, Edwin P.
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       TELECOMMUNICATION INFORMATION:
           TELEPHONE: (650)852-9196
           TELEFAX: (650)496-1204
   INFORMATION FOR SEQ ID NO: 2:
       SEQUENCE CHARACTERISTICS:
           LENGTH: 316 amino acids
           TYPE: amino acid
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Search completed: February 25, 2004, 16:36:10 Job time: 38 secs

GenCore version 5.1.6 Copyright (c) 1993 - 2004 Compugen Ltd.

OM protein - protein search, using sw model

February 25, 2004, 16:25:23; Search time 46 Seconds Run on:

(without alignments)

2174.332 Million cell updates/sec

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Scoring table: BLOSUM62

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Total number of hits satisfying chosen parameters: 1017041

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%

Maximum Match 100%

Listing first 45 summaries

SPTREMBL 25:* Database :

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3: sp fungi:*

4: sp_human:*

5: sp_invertebrate:*
6: sp_mammal:*

7: sp_mhc:*

8: sp organelle:*

9: sp phage:*

10: sp_plant:*

11: sp_rodent:*

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14: sp_unclassified:*

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16: sp bacteriap:*

17: sp archeap:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Query Result

No. Score Match Length DB ID

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7	187.5	11.1	279	11	Q7TMV9	Q7tmv9 mus musculu
8	184.5	10.9	252	11	Q8K3Y8	Q8k3y8 mus musculu
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22	125	7.4	216	6	Q9BEC9	Q9bec9 ochotona pr
23	120.5	7.2	217	6	Q9BEG0	Q9beg0 cyclopes di
24	120.5	7.2	217	6	Q9BEG1	Q9beg1 bradypus tr
25	118.5	7.0	138	6	Q9TTG7	Q9ttg7 aotus lemur
26	117	6.9	244	6	0862Z7	Q862z7 pan troglod
27	116.5	6.9	169	11	Q9WV90	Q9wv90 marmota mon
28	115.5	6.9	154	6	Q8MJ19	Q8mj19 macaca mula
29	114.5	6.8	216	6	Q9BEE0	Q9bee0 macropus ru
30	113.5	6.7	216	6	Q9BEC4	Q9bec4 talpa europ
31	113.5	6.7	237	13	Q8AWC9	Q8awc9 cyprinus ca
32	113	6.7	217	6	Q9BEF4	Q9bef4 cabassous u
33	111	6.6	102	11	Q80Z03	Q80z03 castor cana
34	110.5	6.6	215	6	Q9BEE8	Q9bee8 erinaceus e
35	110	6.5	102	11	Q80Z02	Q80z02 trichys fas
36	109.5	6.5	253	13	Q7T194	Q7t194 acanthopagr
37	109	6.5	102	11	Q80Z05	Q80z05 dipodomys m
38	108	6.4	102	11	Q80Z06	Q80z06 dipus sagit
39	107.5	6.4	222	13	Q7T1U4	Q7t1u4 pagrus majo
40	107.5	6.4	409	5	Q8MY88	Q8my88 drosophila
41	107.5	6.4	409	5	Q8IGD3	Q8igd3 drosophila
42	106.5	6.3	325	5	Q9V5G2	Q9v5g2 drosophila
43	106.5	6.3	415	5	Q8MUJ1	Q8muj1 drosophila
44	106	6.3	3467	5	Q8I218	Q8i218 plasmodium
45	105.5	6.3	103	6	Q864Z0	Q864z0 physeter ca

ALIGNMENTS

```
RESULT 1
Q7ZYX9

ID Q7ZYX9

AC Q7ZYX9;
DT 01-JUN-2003 (TrEMBLrel. 24, Created)
DT 01-JUN-2003 (TrEMBLrel. 24, Last sequence update)
DT 01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
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```
Similar to tumor necrosis factor (Ligand) superfamily, member 10.
DE
    Brachydanio rerio (Zebrafish) (Danio rerio).
OS
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Actinopterygii; Neopterygii; Teleostei; Ostariophysi; Cypriniformes;
OC
OC
    Cyprinidae; Danio.
OX
    NCBI TaxID=7955;
RN
    [1]
RP
    SEQUENCE FROM N.A.
RA
    Strausberg R.;
    Submitted (JAN-2003) to the EMBL/GenBank/DDBJ databases.
RL
    EMBL; BC044336; AAH44336.1; -.
DR
    GO; GO:0016020; C:membrane; IEA.
DR
    GO; GO:0005164; F:tumor necrosis factor receptor binding; IEA.
DR
    GO; GO:0006955; P:immune response; IEA.
DR
    InterPro; IPR006052; TNF family.
DR
DR
    InterPro; IPR008983; TNF like.
    InterPro; IPR003636; TNF subf.
DR
    Pfam; PF00229; TNF; 1.
DR
    ProDom; PD002012; TNF subf; 1.
DR
    SMART; SM00207; TNF; 1.
DR
    PROSITE; PS50049; TNF 2; 1.
DR
    SEQUENCE 317 AA; 35465 MW; 68F76BC1A40DCE9F CRC64;
SQ
                       15.8%; Score 266; DB 13; Length 317;
 Query Match
 Best Local Similarity 26.6%; Pred. No. 1.4e-15;
 Matches 79; Conservative 66; Mismatches 122; Indels 30; Gaps
                                                                    9;
         42 PAASR----SMFVALLGLGLG--QVVCSVALFFYFRAQMDPNRISEDGTHCIYRILRL 93
Qу
                       :::|:: : |: : || | ::: |
         24 PANSRGRDSPSKLWIAMVVIVVVLQIASTTGLFVYL--NMSLSQVKSQGVTEELRCLGL 81
Db
         94 HENADFQDTTLESQDTKLIPDSCRRIKQAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLD 153
Qу
                 82 -LNVLGKDQDIPEDLAQLFGEPCMKLAEGIKAYISKVTDSIISKQTLHAARTRTHSYNTT 140
Db
         154 LAK-RSKLEAQPFAHLTINATDIPS-----GSHKVSLSSWYHDRGWAKISN 198
Qу
             141 GSKFMTTVMQRPSAHLTLSSASDNSRPQSDMHQPQFDLHQSCRHPVHTWANKSFGAHLYN 200
Db
         199 MTFSNGKLIVNQDGFYYLYANICFRHHETS-GDLATEYLQLMVYV-TKTSIKIPSSHTLM 256
Qу
            201 MTLTNGRLRVPQDGRYYLYSQVYFRYPSPSDSDQSSVSHQLVQCIYKKTSYLNPIQ--LL 258
Db
         257 KGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLDPDQDATYFGAFKV 313
Qу
            259 KGVGTKCWAPDAEYALHSVYQGGLFELRAGDEVFVSVSSPTMVYGEDSSSYFGAFRL 315
Db
RESULT 2
O7T1F2
                                    304 AA.
              PRELIMINARY;
                               PRT;
    Q7T1F2
ΙD
    Q7T1F2;
    01-OCT-2003 (TrEMBLrel. 25, Created)
    01-OCT-2003 (TrEMBLrel. 25, Last sequence update)
DT
    01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
DT
    Tumor necrosis factor related apoptosis inducing ligand.
DΕ
    TRAIL.
GN
```

```
OS
    Gallus gallus (Chicken).
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
OC
    Gallus.
OX
    NCBI TaxID=9031;
RN
    [1]
RP
    SEQUENCE FROM N.A.
RC
    TISSUE=Spleen;
    Saved A.A., Horiuchi H.H., Furusawa S., Matsuda H.;
    "Identification and Charachterization of Chicken TNF-Superfamily
RT
    Ligand 8 (CD30 Ligand) and 10 (Tumor Necrosis Factor Related Apoptosis
RT
    Inducing Ligand TRAIL).";
RT
    Submitted (JUL-2003) to the EMBL/GenBank/DDBJ databases.
RL
    EMBL; AB114678; BAC79267.1; -.
DR
    SEQUENCE 304 AA; 34658 MW; DFC128B517747C96 CRC64;
SQ
 Query Match
                       15.7%; Score 265; DB 13; Length 304;
 Best Local Similarity 27.3%; Pred. No. 1.6e-15;
 Matches 82; Conservative 56; Mismatches 126; Indels 36; Gaps
                                                                    12;
          38 PHQPPAASRSMFVALLGLGLGQVVCSVALFFYFRAQMDP--NRISEDGTHCI--YRILRL 93
Qу
            3 PAGGPSPAHTCGAVLVAAVLLQSVCVAVTYIYFTNELKQLWDTYSRSGTACLTGEELGDL 62
Db
          94 HENADFODTTLESODTKLIPDSCRRIKQAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLD 153
QУ
             :| | :||:| : | ::| : : : ::|
          63 IQNLD----VVESKDR--VADPCWQVKWHLGKLIKKMMSRI-----LQENMSAINGDRTQ 111
Db
         154 -LAKRSKLEAQP----FAHLTINATDIPSGSHKV-----SLSSWYHD-RGWAKISNM 199
QУ
             | | | : : | :
         112 ALSRRDEPPOGPTLRIAAHLTGSSKRSSASPHNYLSYRGIGHKIHSWESSRRGHSFLYNV 171
Db
         200 TFSNGKLIVNQDGFYYLYANICFRHHET----SG--DLATEYLQLMVYVTKTSIKIPSSH 253
QУ
               172 ELWNGELVVPQTGFYYIYSQTYFRFRENEDEDSGLLERIKNPKQLVQYIYKLT-NYPDPI 230
Db
         254 TLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLDPDQDATYFGAFKV 313
Qу
                 231 LLMKSARTSCWSKKAEYGLYSVYQGGVFQLKREDRIFVSVSNSDIVDMDKEASFFGAFMI 290
Db
RESULT 3
O9DDZ5
             PRELIMINARY; PRT; 214 AA.
    Q9DDZ5
ΙD
    Q9DDZ5;
AC
    01-MAR-2001 (TrEMBLrel. 16, Created)
DT
    01-MAR-2001 (TrEMBLrel. 16, Last sequence update)
    01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
DT
DE
    TRAIL-like protein.
GN
    TNFSF10L.
    Brachydanio rerio (Zebrafish) (Danio rerio).
OS
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Actinopterygii; Neopterygii; Teleostei; Ostariophysi; Cypriniformes;
OC
    Cyprinidae; Danio.
OX
    NCBI TaxID=7955;
RN
    [1]
RP
    SEQUENCE FROM N.A.
```

```
RA
    Bobe J., Goetz F.W.;
RT
    "Molecular cloning and expression of a TNF receptor and two TNF
RT
    ligands in the fish ovary.";
    Comp. Biochem. Physiol. B, Comp. Biochem. 129:475-481(2001).
RL
    EMBL; AF250041; AAG47640.1; -.
DR
    HSSP; P50591; 1D2Q.
DR
DR
    ZFIN; ZDB-GENE-010801-1; tnfsf101.
DR
    GO; GO:0016020; C:membrane; IEA.
DR
    GO; GO:0005164; F:tumor necrosis factor receptor binding; IEA.
    GO; GO:0006955; P:immune response; IEA.
DR
    InterPro; IPR006052; TNF family.
    InterPro; IPR008983; TNF like.
DR
    InterPro; IPR003636; TNF subf.
DR
    Pfam; PF00229; TNF; 1.
DR
DR
    ProDom; PD002012; TNF subf; 1.
    SMART; SM00207; TNF; 1.
DR
DR
    PROSITE; PS50049; TNF 2; 1.
    SEQUENCE 214 AA; 24093 MW; 98C002474FF691AA CRC64;
SO
 Query Match 14.3%; Score 240.5; DB 13; Length 214; Best Local Similarity 28.6%; Pred. No. 1.6e-13;
 Matches 61; Conservative 50; Mismatches 83; Indels 19; Gaps
                                                                         5;
         118 RIKQAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAK-RSKLEAQPFAHLTINATDIP 176
Qу
             ::::::
                          |: | : | :
                                         :| : : :| |||:::
           2 KLAEGIKAYISKVTDSIISKQTLHAARTQTHSYNTTGSKFMTTVMQRPSAHLTLSSASDN 61
Db
         177 S----GSHKVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICF 222
QУ
                            62 SRPQSDMHQPQFDLHQSCRHPVHTWANKSFGAHLYNMTLTNGRLRVPQDGRYYLYSQVYF 121
Db
         223 RHHETS-GDLATEYLQLMVYV-TKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGF 280
QУ
             122 RYPSPSDSDQSSVSHQLVQCIYKKTSYLNPIQ--LLKGVGTKCWAPDAEYALHSVYQGGL 179
Db
         281 FKLRSGEEISIEVSNPSLLDPDQDATYFGAFKV 313
Qу
             |:||:|:|: : ||:|::: : ::|||||
         180 FELRAGDEVFVSVSSPTMVYGEDSSSYFGAFRL 212
Db
RESULT 4
Q90WT9
ΙD
    Q90WT9
               PRELIMINARY; PRT; 287 AA.
    Q90WT9;
AC
    01-DEC-2001 (TrEMBLrel. 19, Created)
DT
    01-DEC-2001 (TrEMBLrel. 19, Last sequence update)
DT
    01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
DT
    TNF-related apoptosis inducing ligand.
DE
    Gallus gallus (Chicken).
OS
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
OC
OC
    Gallus.
    NCBI TaxID=9031;
OX
RN
    [1]
RP
    SEQUENCE FROM N.A.
RA
     Bridgham J.T., Johnson A.L.;
     "TNF-related apoptosis inducing ligand (TRAIL) expression in the hen
RT
```

```
RT
    ovary.";
RL
    Submitted (OCT-2001) to the EMBL/GenBank/DDBJ databases.
DR
    EMBL; AY057941; AAL23702.1; -.
DR
    HSSP; 035235; 1IQA.
    GO; GO:0016020; C:membrane; IEA.
DR
DR
    GO; GO:0005164; F:tumor necrosis factor receptor binding; IEA.
DR
    GO; GO:0006955; P:immune response; IEA.
DR
    InterPro; IPR006053; TNF abc.
DR
    InterPro; IPR006052; TNF family.
    InterPro; IPR008983; TNF like.
DR
    InterPro; IPR003636; TNF subf.
DR
    Pfam; PF00229; TNF; 1.
DR
    PRINTS; PR01234; TNECROSISFCT.
DR
DR
    ProDom; PD002012; TNF subf; 1.
    SMART; SM00207; TNF; 1.
DR
DR
    PROSITE; PS50049; TNF 2; 1.
SO
    SEQUENCE 287 AA; 32092 MW; DB06E1C95087B108 CRC64;
 Query Match 12.8%; Score 216.5; DB 13; Length 287; Best Local Similarity 24.7%; Pred. No. 3.5e-11;
 Matches 61; Conservative 57; Mismatches 104; Indels 25; Gaps
                                                                       6;
          80 SEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIKQAFQGAVQKELQHIVGSQH 139
Qу
            Db
          51 SSEELRCLQLINQQQEGSNLEEL-----ISNQSCLKLANTIKAYVATVTENVISRSV 102
         140 I-RAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIP-----SGSHKVSLSSW 187
ΟV
             : |:|: : | :| :| :| || :
                                                         | | : ::: |
         103 VNEAQKSYFNISEGQVA--TKTLGKPSAHLIFRPQNPAQDGSSRRFGNLSQSCRHAITRW 160
Db
         188 YHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMVYVT-KTS 246
QУ
                  | | | : : | | | |
         161 EDSTIHSHLQNITYRDGRLRVNQAGKYYVYSQIYFRYSRDGAGARVSVPQLVQCINWKTS 220
Db
Qу
         247 IKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLDPDODAT 306
              Db
         221 YSQPI--LLLKGVGTKCWAPEAEYGLHALYQGGLFELKAGDELFVSVSSLAIDYSDAAAS 278
         307 YFGAFKV 313
Qу
             | | | | | : :
         279 YFGAFRL 285
Db
RESULT 5
Q8K3G0
              PRELIMINARY; PRT; 287 AA.
    Q8K3G0
AC
    Q8K3G0;
    01-OCT-2002 (TrEMBLrel. 22, Created)
DT
    01-OCT-2002 (TrEMBLrel. 22, Last sequence update)
DΤ
    01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
DT
    TNF-related apoptosis inducing ligand.
DE
    Rattus norvegicus (Rat).
OS
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
OX
    NCBI TaxID=10116;
RN
    [1]
RP
    SEQUENCE FROM N.A.
```

```
RC
    STRAIN=DA;
RA
    Mueller A.M., Giegerich G.;
     "Rattus norvegicus TNF-related apoptosis inducing ligand (TRAIL).";
RT
RΤ
    Submitted (MAY-2002) to the EMBL/GenBank/DDBJ databases.
DR
    EMBL; AY115578; AAM49797.1; -.
DR
    GO; GO:0016020; C:membrane; IEA.
    GO; GO:0005164; F:tumor necrosis factor receptor binding; IEA.
DR
    GO; GO:0006955; P:immune response; IEA.
DR
DR
    InterPro; IPR006052; TNF_family.
DR
    InterPro; IPR008983; TNF like.
DR
    InterPro; IPR003636; TNF subf.
DR
    Pfam; PF00229; TNF; 1.
DR
    ProDom; PD002012; TNF subf; 1.
    SMART; SM00207; TNF; 1.
    PROSITE; PS00251; TNF 1; 1.
DR
DR
    PROSITE; PS50049; TNF 2; 1.
SO
    SEQUENCE 287 AA; 32979 MW; CA4F5B5D7C833FEC CRC64;
  Query Match
                     12.8%; Score 215.5; DB 11; Length 287;
  Best Local Similarity 24.2%; Pred. No. 4.3e-11;
 Matches 73; Conservative 59; Mismatches 113; Indels 57; Gaps
         42 PAASRSMFVALLGLGLGQVV---CSVAL-FFYFRAQMD--PNRISEDGTHCIYRILRLHE 95
Qу
            10 PSFSQHFTMTVICIVLLQVLLQALTVAVTYMYFNNEVKQLQDNYSKIGLACFSK----E 64
Db
         96 NADFQDTTLESQDTKLIPDSCRRIKQAFQGAVQKELQHIVGSQHIRA-EKAMVDGSWLDL 154
Qу
            Db
         65 DGDFWDST----DEGILNRPCLQVK------RQLYQLIEEVTLRTFEKT-----IST 106
        155 AKRSKLEAQPF-----AHLT----INATDIPSGSHKVSL----SSWYHD-RGWA 194
Qу
               Db
        107 VPEKQLSTPPLPRGRRPQRVAAHITGITRRSNLALIPISKDGKTLGQKIETWESSRRGHS 166
        195 KISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLAT-----EYLQLMVYVTKTSIK 248
Qу
            Db
        167 FLNHVHLRNGELVIQEEGLYYIYSQTYYRFKEAKEASKTVSKDGGRIKQMVQYIYKYT-S 225
        249 IPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLDPDQDATYF 308
Qу
                Db
        226 YPDPILLMKSARNSCWSREAEYGLYSIYQGGLFELKENDRIFVSVTNEHLMDLDHEASFF 285
        309 GA 310
Qу
           Db
        286 GA 287
RESULT 6
Q861W5
ID
   Q861W5
              PRELIMINARY; PRT; 280 AA.
AC
    Q861W5;
   01-JUN-2003 (TrEMBLrel. 24, Created)
DT
    01-JUN-2003 (TrEMBLrel. 24, Last sequence update)
DT
    01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
DΕ
   Fas ligand.
OS Felis silvestris catus (Cat).
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
```

```
Mammalia; Eutheria; Carnivora; Fissipedia; Felidae; Felis.
OX
    NCBI TaxID=9685;
RN
     [1]
RP
     SEQUENCE FROM N.A.
RX
    MEDLINE=99053606; PubMed=9839871;
    Mizuno T., Endo Y., Momoi Y., Goto Y., Nishimura Y., Tsubota K.,
RA
RA
    Mikami T., Ohno K., Watari T., Tsujimoto H., Hasegawa A.;
     "Molecular cloning of feline Fas antigen and Fas ligand cDNAs.";
RΤ
RL
    Vet. Immunol. Immunopathol. 65:161-172(1998).
DR
    EMBL; AB009280; BAC76426.1; -.
DR
    GO; GO:0005576; C:extracellular; IEA.
DR
    GO; GO:0016020; C:membrane; IEA.
    GO; GO:0005164; F:tumor necrosis factor receptor binding; IEA.
DR
    GO; GO:0006915; P:apoptosis; IEA.
    GO; GO:0006955; P:immune response; IEA.
DR
    GO; GO:0007165; P:signal transduction; IEA.
DR
    InterPro; IPR008064; Fas ligand.
DR
    InterPro; IPR006053; TNF abc.
DR
    InterPro; IPR006052; TNF family.
DR
    InterPro; IPR008983; TNF like.
    InterPro; IPR003636; TNF subf.
DR
    Pfam; PF00229; TNF; 1.
DR
    PRINTS; PR01681; FASLIGAND.
DR
    PRINTS; PR01234; TNECROSISFCT.
DR
    ProDom; PD002012; TNF subf; 1.
DR
    SMART; SM00207; TNF; 1.
DR
    PROSITE; PS00251; TNF 1; 1.
    PROSITE; PS50049; TNF 2; 1.
SQ
    SEQUENCE 280 AA; 31361 MW; 6AA7E2DE1F1A6B5C CRC64;
  Query Match 11.5%; Score 194.5; DB 6; Length 280; Best Local Similarity 22.8%; Pred. No. 3.3e-09;
 Matches 74; Conservative 40; Mismatches 98; Indels 113; Gaps
         20 GGPG----APHEGPLHAPPPPAPHQPPAASRSM-----FVALLGLG 56
Qу
           Db
         38 GRPGQRRPPPPPPTLPPPPPPPPPPLPPLPPLKTRRDHNTGLCLLVMFFMVLVALVGLG 97
         57 LGQVVCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSC 116
Qу
           :| | |
                                           | |: :::| :
         98 LG-----KELAELRESTSQKH------ 121
Db
        117 RRIKQAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLT--INATD 174
Qy
                    | | | : : | : : | |
                                            | : | | | |
        122 -----ELRKVAHLTGKPNSRS 156
Db
        175 IPSGSHKVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATE 234
QУ
            Db
        157 IP-----LEWEDTYGIALVSGVKYKKGGLVINDTGMYFVYSKVNFRGQSCN----NQ 204
        235 YLQLMVYVTKTSIKIPSSHTLMKGGSTKY-----WSGNSEFHFYSINVGGFFKLRSGEE 288
Qу
            Db
        205 PLNHKVYMRNS--KYPQDLVLMEGKMMNYCTTGQMWARSS-----YLGAVFNLTSADH 255
Qу
        289 ISIEVSNPSLLDPDQDATYFGAFKV 313
            :: || || :: |:|| :|:
        256 LYVNVSELSLVSFEESKTFFGLYKL 280
```

```
RESULT 7
Q7TMV9
ID
     Q7TMV9
                PRELIMINARY; PRT; 279 AA.
AC
     Q7TMV9;
     01-OCT-2003 (TrEMBLrel. 25, Created)
DT
DT
     01-OCT-2003 (TrEMBLrel. 25, Last sequence update)
DT
     01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
DE
     Tnfsf6 protein.
OS
     Mus musculus (Mouse).
OC
     Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
     Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX
     NCBI TaxID=10090;
RN
     [1]
RP
     SEQUENCE FROM N.A.
RC
     STRAIN=C57BL/6NCr; TISSUE=Hematopoietic Stem Cell;
RX
     MEDLINE=22388257; PubMed=12477932;
RA
     Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
RA
     Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
RA
     Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
     Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
RA
     Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
RA
     Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,
RA
     Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
RA
     Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
RA
     Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
RA
RA
     Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
RA
    Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
     Fahey J., Helton E., Ketteman M., Madan A., Rodrigues S., Sanchez A.,
RA
    Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
RA
RA
    Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,
RA
    Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M., Butterfield Y.S.,
RA
    Krzywinski M.I., Skalska U., Smailus D.E., Schnerch A., Schein J.E.,
RA
    Jones S.J., Marra M.A.;
RT
    "Generation and initial analysis of more than 15,000 full-length human
RТ
    and mouse cDNA sequences.";
RL
    Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
RN
     [2]
RP
    SEQUENCE FROM N.A.
RC
    STRAIN=C57BL/6NCr; TISSUE=Hematopoietic Stem Cell;
RA
    Strausberg R.;
RL
    Submitted (MAY-2003) to the EMBL/GenBank/DDBJ databases.
    EMBL; BC052866; AAH52866.1; -.
DR
SO
    SEQUENCE 279 AA; 31416 MW; C2972E2728FBBB7B CRC64;
 Query Match
                        11.1%; Score 187.5; DB 11; Length 279;
 Best Local Similarity 21.7%; Pred. No. 1.4e-08;
 Matches
          70; Conservative 46; Mismatches 105; Indels 101; Gaps
Qу
          13 RGSEEMGGGPGAPHEGPLHAPPPPAPHQP-----PAASRSMFVALLGLGL 57
             Db
          38 RGPDQRRPPPPPPPVSPLPPPSQPLPLPPLTPLKKKDHNTNLWLPVVFFMVLVALVGMGL 97
          58 GQVVCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCR 117
Qу
                :1:: |
          98 G------ 105
Db
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118 RIKQAFQGAVQKELQHI--VGSQHIRA---EKAMVDGSWLDLAKRSKLEAQPFAHLTINA 172
Qy
                      1111 : :1:: ||::|
                                                        | | : | | | |
          106 -----QKELAELREFTNQSLKVSSFEKQIANPS----TPSEKKEPRSVAHLTGN- 150
Db
          173 TDIPSGSHKVSLS-SWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDL 231
Qу
                    Db
          151 -----PHSRSIPLEWEDTYGTALISGVKYKKGGLVINETGLYFVYSKVYFRGQSCN--- 201
Qy
          232 ATEYLQLMVYVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISI 291
               202 -NQPLNHKVYMRNS--KYPEDLVLMEEKRLNYCT-TGQIWAHSSHLGAVFNLTSADHLYV 257
Db
Qу
         292 EVSNPSLLDPDQDATYFGAFKV 313
              :| ||:: :: |:|| :|:
Db
         258 NISQLSLINFEESKTFFGLYKL 279
RESULT 8
Q8K3Y8
ID
     Q8K3Y8
               PRELIMINARY; PRT; 252 AA.
АC
     Q8K3Y8;
DΤ
     01-OCT-2002 (TrEMBLrel. 22, Created)
     01-OCT-2002 (TrEMBLrel. 22, Last sequence update)
     01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
DT
DE
    TNF superfamily ligand TL1A.
GN
    TNFSF15.
    Mus musculus (Mouse).
OS
OC
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
    Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OC
OX
    NCBI TaxID=10090;
RN
    [1]
RP
    SEQUENCE FROM N.A.
RC
    STRAIN=BALB/c;
RX
    MEDLINE=21909416; PubMed=11911831;
RA
    Migone T.S., Zhang J., Luo X., Zhuang L., Chen C., Hu B., Hong J.S.,
    Perry J.W., Chen S.F., Zhou J.X., Cho Y.H., Ullrich S., Kanakaraj P.,
RA
RA
    Carrell J., Boyd E., Olsen H.S., Hu G., Pukac L., Liu D., Ni J.,
RA
    Kim S., Gentz R., Feng P., Moore P.A., Ruben S.M., Wei P.;
RT
    "TL1A is a TNF-like ligand for DR3 and TR6/DcR3 and functions as a T
RT
    cell costimulator.";
RL
    Immunity 16:479-492(2002).
DR
    EMBL; AF520786; AAM77367.1; -.
DR
    MGD; MGI:2180140; Tnfsf15.
    GO; GO:0016020; C:membrane; IEA.
DR
    GO; GO:0005164; F:tumor necrosis factor receptor binding; IEA.
    GO; GO:0006955; P:immune response; IEA.
DR
DR
    InterPro; IPR006053; TNF abc.
DR
    InterPro; IPR006052; TNF family.
DR
    InterPro; IPR008983; TNF like.
DR
    InterPro; IPR003636; TNF subf.
DR
    Pfam; PF00229; TNF; 1.
    PRINTS; PR01234; TNECROSISFCT.
DR
    ProDom; PD002012; TNF subf; 1.
DR
    SMART; SM00207; TNF; 1.
    PROSITE; PS50049; TNF 2; 1.
DR
SQ
    SEQUENCE 252 AA; 27723 MW; BB901C9350119E0F CRC64;
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Query Match
                       10.9%; Score 184.5; DB 11; Length 252;
  Best Local Similarity 26.2%; Pred. No. 2.3e-08;
  Matches 64; Conservative 39; Mismatches 100; Indels 41; Gaps
                                                                    10;
Qу
         105 ESQDTKLIPDSCRRIKQAFQGAVQK-----ELQHIVG-SQHIRAEKAMVDGSW 151
                 :::|: || :| :
                                                : | | : | : | |
          11 EGVPVEVLPEGCRHRPEARAGLAARSKACLALTCCLLSFPILAGLSTLLMAGQLRVPGK- 69
Db
Qу
         152 LDLAKRSKLE-----AQPFAHLTI-NATDIPSGSHKVSLSSWYHDRGWAK 195
             | |: |
                                   Db
          70 -DCMLRAITEERSEPSPQQVYSPPRGKPRAHLTIKKQTPAPHLKNQLSALHWEHDLGMAF 128
         196 ISN-MTFSNGKLIVNQDGFYYLYANICFR-HHETSGDLA----TEYLQLMVYVTKTSIK 248
QУ
              Db
         129 TKNGMKYINKSLVIPESGDYFIYSQITFRGTTSVCGDISRGRRPNKPDSITVVITKVADS 188
         249 IPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD-PDQDATY 307
Qу
             Db
         189 YPEPARLLTGSKSVCEISNN--WFQSLYLGAMFSLEEGDRLMVNVSDISLVDYTKEDKTF 246
Qу
         308 FGAF 311
            1111
Db
         247 FGAF 250
RESULT 9
080YZ0
ID
    Q80YZ0
              PRELIMINARY; PRT; 252 AA.
    Q80YZ0;
    01-JUN-2003 (TrEMBLrel. 24, Created)
    01-JUN-2003 (TrEMBLrel. 24, Last sequence update)
DT
    01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
DT
DE
    BM20K13.3 (Tumor necrosis factor (Ligand) superfamily, member
DE
    15).
GN
    TNFSF15.
OS
    Mus musculus (Mouse).
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX
    NCBI TaxID=10090;
RN
    [1]
    SEQUENCE FROM N.A.
RP
RA
    Sycamore N.;
RL
    Submitted (MAR-2003) to the EMBL/GenBank/DDBJ databases.
   EMBL; AL691468; CAD83021.1; -.
DR
    GO; GO:0016020; C:membrane; IEA.
DR
    GO; GO:0005164; F:tumor necrosis factor receptor binding; IEA.
DR
    GO; GO:0006955; P:immune response; IEA.
DR
DR
    InterPro; IPR006053; TNF abc.
DR InterPro; IPR006052; TNF family.
DR InterPro; IPR008983; TNF like.
DR InterPro; IPR003636; TNF subf.
DR Pfam; PF00229; TNF; 1.
DR
   PRINTS; PR01234; TNECROSISFCT.
DR
   ProDom; PD002012; TNF subf; 1.
    SMART; SM00207; TNF; 1.
DR
   PROSITE; PS50049; TNF 2; 1.
DR
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SQ SEQUENCE 252 AA; 27725 MW; A63ABDCC9E969E0F CRC64;
  Query Match
                       10.7%; Score 179.5; DB 11; Length 252;
  Best Local Similarity 25.8%; Pred. No. 6.5e-08;
  Matches 63; Conservative 40; Mismatches 100; Indels 41; Gaps
         105 ESQDTKLIPDSCRRIKQAFQGAVQK-----ELQHIVG-SQHIRAEKAMVDGSW 151
Qy
            11 EGVPVEVLPEGCRHRPEARAGLAARSKACLALTCCLLSFPILAGLSTLLMAGQLRVPGK- 69
Db
         152 LDLAKRSKLE------AQPFAHLTI-NATDIPSGSHKVSLSSWYHDRGWAK 195
Qу
             1: 1:
                       70 -DCMLRAITEERSEPSPQQVYSPPRGKPRAHLTIKKQTPAPHLKNQLSALHWEHDLGMAF 128
Db
Qу
         196 ISN-MTFSNGKLIVNQDGFYYLYANICFR-HHETSGDLA----TEYLQLMVYVTKTSIK 248
              Db
         129 TKNGMKYINKSLVIPESGDYFIYSQITFRGTTSVCGDISRGRRPNKPDSITMVITKVADS 188
         249 IPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD-PDQDATY 307
QУ
                 Db
         189 YPEPARLLTGSKSVCEISNN--WFQSLYLGATFSLEEGDRLMVNVSDISLVDYTKEDKTF 246
        308 FGAF 311
Qу
            Db
         247 FGAF 250
RESULT 10
Q8K3Y7
               PRELIMINARY; PRT; 252 AA.
ID
    Q8K3Y7
    01-OCT-2002 (TrEMBLrel. 22, Created)
    01-OCT-2002 (TrEMBLrel. 22, Last sequence update)
DT
DT
    01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
DE
    TNF superfamily ligand TL1A.
GN
    TNFSF15.
OS
    Rattus norvegicus (Rat).
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
OC
OX
    NCBI TaxID=10116;
RN
    [1]
RΡ
    SEQUENCE FROM N.A.
RC
    STRAIN=Sprague-Dawley;
RX
    MEDLINE=21909416; PubMed=11911831;
    Migone T.S., Zhang J., Luo X., Zhuang L., Chen C., Hu B., Hong J.S.,
RA
    Perry J.W., Chen S.F., Zhou J.X., Cho Y.H., Ullrich S., Kanakaraj P.,
RA
    Carrell J., Boyd E., Olsen H.S., Hu G., Pukac L., Liu D., Ni J.,
RA
    Kim S., Gentz R., Feng P., Moore P.A., Ruben S.M., Wei P.;
RA
    "TL1A is a TNF-like ligand for DR3 and TR6/DcR3 and functions as a T
RT
RT
    cell costimulator.";
RL
    Immunity 16:479-492(2002).
    EMBL; AF520787; AAM77368.1; -.
DR
    GO; GO:0016020; C:membrane; IEA.
    GO; GO:0005164; F:tumor necrosis factor receptor binding; IEA.
DR
DR
    GO; GO:0006955; P:immune response; IEA.
DR
    InterPro; IPR006053; TNF abc.
    InterPro; IPR006052; TNF family.
DR
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DR
     InterPro; IPR008983; TNF like.
DR
     InterPro; IPR003636; TNF subf.
DR
     Pfam; PF00229; TNF; 1.
DR
     PRINTS; PR01234; TNECROSISFCT.
     ProDom; PD002012; TNF subf; 1.
DR
DR
     SMART; SM00207; TNF; \overline{1}.
DR
     PROSITE; PS50049; TNF 2; 1.
SQ
     SEQUENCE 252 AA; 28029 MW; 7789E6556D46F293 CRC64;
  Query Match 10.5%; Score 177.5; DB 11; Length 252; Best Local Similarity 25.1%; Pred. No. 9.8e-08;
  Matches 62; Conservative 43; Mismatches 99; Indels 43; Gaps
Qу
         105 ESQDTKLIPDSCRRIKQAFQGAVQKELQHI-----VGSQHIRAEK 144
             |: :::|: || ::| | : :
                                                           | | :
Db
          11 EAVPVEMLPEGCRHRREARTGLAARSKACLALTCCLLSFPILAGLSTLLMTGQLRIPGKD 70
         145 AMVDGSWLDLAKRSKLEAQPF-----AHLTI-NATDIPSGSHKVSLSSWYHDRGWA 194
Qу
             Db
          71 CMFP---TVTEERSAPSAQPVYTPSRDKPKAHLTIMRQTPVPHLKNELAALHWENNLGMA 127
         195 KISN-MTFSNGKLIVNQDGFYYLYANICFRHHETS-GDLA----TEYLQLMVYVTKTSI 247
Qу
                Db
         128 FTKNRMNYTNKFLVIPESGDYFIYSQITFRGTTSECGDISRVRRPKKPDSITVVITKVAD 187
         248 KIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD-PDQDAT 306
Qy
              Db
         188 SYPEPAHLLTG--TKSVCEISSNWFQPIYLGAMFSLEEGDRLMVNVSDISLVDYTKEDKT 245
         307 YFGAFKV 313
QУ
             : | | | | :
Db
         246 FFGAFLI 252
RESULT 11
O8NFE9
TD
    Q8NFE9
              PRELIMINARY;
                              PRT; 251 AA.
АC
    Q8NFE9;
DT
    01-OCT-2002 (TrEMBLrel. 22, Created)
DT
    01-OCT-2002 (TrEMBLrel. 22, Last sequence update)
    01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
DT
DE
    TNF superfamily ligand TL1A.
GN
    TNFSF15.
OS
    Homo sapiens (Human).
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OC
OX
    NCBI TaxID=9606;
RN
    [1]
RΡ
    SEQUENCE FROM N.A.
RX
    MEDLINE=21909416; PubMed=11911831;
    Migone T.S., Zhang J., Luo X., Zhuang L., Chen C., Hu B., Hong J.S.,
RA
    Perry J.W., Chen S.F., Zhou J.X., Cho Y.H., Ullrich S., Kanakaraj P.,
RA
RA
    Carrell J., Boyd E., Olsen H.S., Hu G., Pukac L., Liu D., Ni J.,
    Kim S., Gentz R., Feng P., Moore P.A., Ruben S.M., Wei P.;
RA
    "TL1A is a TNF-like ligand for DR3 and TR6/DcR3 and functions as a T
RT
RT
    cell costimulator.";
RL
    Immunity 16:479-492(2002).
```

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EMBL; AF520785; AAM77366.1; -.
DR
     GO; GO:0016020; C:membrane; IEA.
DR
     GO; GO:0005164; F:tumor necrosis factor receptor binding; IEA.
DR
     GO; GO:0006955; P:immune response; IEA.
DR
     InterPro; IPR006053; TNF abc.
DR
     InterPro; IPR006052; TNF family.
DR
     InterPro; IPR008983; TNF like.
    InterPro; IPR003636; TNF subf.
DR
DR
     Pfam; PF00229; TNF; 1.
    PRINTS; PR01234; TNECROSISFCT.
DR
DR
    ProDom; PD002012; TNF subf; 1.
DR
    SMART; SM00207; TNF; 1.
DR
     PROSITE; PS50049; TNF 2; 1.
SO
    SEQUENCE
             251 AA; 28087 MW; 65ED70E367E3446D CRC64;
  Query Match
                         9.3%; Score 156.5; DB 4; Length 251;
  Best Local Similarity 28.0%; Pred. No. 7.7e-06;
         45; Conservative 33; Mismatches 66; Indels
                                                           17; Gaps
         163 QPFAHLT-INATDIPSGSHKVSLSSWYHDRGWAKISN-MTFSNGKLIVNQDGFYYLYANI 220
QУ
             Db
          94 KPRAHLTVVRQTPTQHFKNQFPALHWEHELGLAFTKNRMNYTNKFLLIPESGDYFIYSOV 153
         221 CFRHHETSGDLATEYLQ-----LMVYVTKTSIKIPSSHTLMKGGSTKYWSGNSEFH 271
QУ
                                : | : | | : | : | : |
              | | : | : | |
Dh
         154 TFRGMTSE---CSEIRQAGRPNKPDSITVVITKVTDSYPEPTQLLMGTKSVCEVGSN--W 208
         272 FYSINVGGFFKLRSGEEISIEVSNPSLLD-PDODATYFGAF 311
Qy
             Dh
         209 FQPIYLGAMFSLQEGDKLMVNVSDISLVDYTKEDKTFFGAF 249
RESULT 12
Q99ND1
ΙD
    Q99ND1
                PRELIMINARY;
                                 PRT;
                                        215 AA.
АC
    Q99ND1;
DT
    01-JUN-2001 (TrEMBLrel. 17, Created)
    01-JUN-2001 (TrEMBLrel. 17, Last sequence update)
DT
    01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
DT
DE
    Tumor necrosis factor (Fragment).
    TNFA.
GN
OS
    Tamiasciurus hudsonicus (American red squirrel).
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
    Mammalia; Eutheria; Rodentia; Sciurognathi; Sciuridae; Sciurinae;
OC
OC
    Tamiasciurus.
OX
    NCBI_TaxID=10009;
RN
    [1]
RP
    SEQUENCE FROM N.A.
RA
    van Dijk M.A.M., de Jong W.W.;
RT
    "Indels indicate that rodents are monophyletic and lagomorphs are
RT
    their sister group.";
    Submitted (FEB-2000) to the EMBL/GenBank/DDBJ databases.
RL
DR
    EMBL; AJ286824; CAC28540.1; -.
DR
    HSSP; P06804; 2TNF.
DR
    GO; GO:0016020; C:membrane; IEA.
DR
    GO; GO:0005164; F:tumor necrosis factor receptor binding; IEA.
    GO; GO:0006955; P:immune response; IEA.
```

```
InterPro; IPR006053; TNF abc.
    InterPro; IPR006052; TNF family.
DR
    InterPro; IPR008983; TNF like.
DR
    InterPro; IPR003636; TNF subf.
DR
    Pfam; PF00229; TNF; 1.
DR
    PRINTS; PR01234; TNECROSISFCT.
DR
    ProDom; PD002012; TNF subf; 1.
DR
    SMART; SM00207; TNF; 1.
DR
    PROSITE; PS00251; TNF 1; 1.
DR
DR
    PROSITE; PS50049; TNF 2; 1.
FT
    NON TER 1 1
    NON TER
               215 215
FT
    SEQUENCE 215 AA; 23739 MW; 36441309CA5E9898 CRC64;
SO
 Query Match
                        8.3%; Score 139.5; DB 11; Length 215;
 Best Local Similarity 26.5%; Pred. No. 0.00021;
 Matches 40; Conservative 27; Mismatches 51; Indels 33; Gaps 5;
         163 QPFAHLTINATDIPSGSHKVSLSSWYHDRGWAKISN-MTFSNGKLIVNQDGFYYLYANIC 221
Qу
             79 KPVAHVVANQTE-----EQLQWLSRRANALLANGMELIDNQLVVPADGLYLIYSQVL 130
Db
         222 FRHHETSGDLATEYLQLMVYVTK-----TSIKIPSSHTLMKGGSTKYWSGNSE 269
Qу
             1: | : |: | :: | :: | :: |
                                                     ::|
                                                             1 1
Db
         131 FK-----GQGCSSYVLLTHTVSRFAVSYQDKVNLLSAIKSPCPKESLEGAEFKPW---- 180
Qу
         270 FHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
              : | :|| |:|: |: :| ||: ||
Db
         181 --YEPIYLGGVFELQKGDRLSAEVNLPSYLD 209
RESULT 13
Q91ZL4
             PRELIMINARY; PRT; 156 AA.
ΙD
    Q91ZL4
AC
    091ZL4;
    01-DEC-2001 (TrEMBLrel. 19, Created)
    01-DEC-2001 (TrEMBLrel. 19, Last sequence update)
DT
    01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
DT
DE
    Tumor necrosis factor alpha (Fragment).
OS
    Sigmodon hispidus (Hispid cotton rat).
OC
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
    Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Sigmodontinae;
OC
OC
    Sigmodon.
OX
    NCBI TaxID=42415;
RN
    [1]
RΡ
    SEQUENCE FROM N.A.
RA
    Blanco J.C., Pletneva L.M., Prince G.A.;
RT
    "Sigmodon hispidus cytokines, chemokines and interferons.";
    Submitted (SEP-2001) to the EMBL/GenBank/DDBJ databases.
RL
    EMBL; AF421388; AAL18818.1; -.
DR
    GO; GO:0016020; C:membrane; IEA.
DR
    GO; GO:0005164; F:tumor necrosis factor receptor binding; IEA.
DR
DR
    GO; GO:0006955; P:immune response; IEA.
DR
    InterPro; IPR006053; TNF abc.
DR
    InterPro; IPR006052; TNF family.
DR
    InterPro; IPR008983; TNF like.
    InterPro; IPR003636; TNF subf.
```

```
DR
    Pfam; PF00229; TNF; 1.
DR
    PRINTS; PR01234; TNECROSISFCT.
    ProDom; PD002012; TNF subf; 1.
    SMART; SM00207; TNF; 1.
DR
    PROSITE; PS00251; TNF 1; 1.
DR
DR
    PROSITE; PS50049; TNF 2; 1.
    NON TER
FT
              1
                       - 1
SQ
    SEQUENCE 156 AA; 17303 MW; DC565F3BC3C826E4 CRC64;
  Query Match
                        8.2%; Score 137.5; DB 11; Length 156;
  Best Local Similarity 27.0%; Pred. No. 0.0002;
  Matches 43; Conservative 25; Mismatches 68; Indels 23; Gaps
                                                                       7;
Qу
         160 LEAQPFAHLTINATDIPSGSHKVSLSSWYHDRGWAKISN-MTFSNGKLIVNQDGFYYLYA 218
            Db
           8 LSDKPVAHVVAN-----QQAEEQLEWLSQRANALLANGMDLRNNQLVIPADGLYLVYS 60
         219 NICFRHHETSG-DLATEYLQLMV--YVTK----TSIKIPSSHTLMKGGSTKYWSGNSEFH 271
Qу
              Db
          61 QVLFKGLGRSNCELLTHTVSRIAVSYEDKVNLLSAIKSPCPKETPQGAELKPW----- 113
Qу
         272 FYSINVGGFFKLRSGEEISIEVSNPSLLD-PDQDATYFG 309
            Db
         114 YEPIYLGGVFQLEKGDRLSAEVNHPKYLDFAESGQVYFG 152
RESULT 14
Q80XA4
ID
   Q80XA4
              PRELIMINARY; PRT; 232 AA.
AC
    O80XA4;
    01-JUN-2003 (TrEMBLrel. 24, Created)
    01-JUN-2003 (TrEMBLrel. 24, Last sequence update)
DT
    01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
\mathsf{DT}
DE
    Tumor necrosis factor precursor (Fragment).
GN
OS
    Peromyscus maniculatus (Deer mouse).
OC
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Sigmodontinae;
OC
    Peromyscus.
OX
    NCBI TaxID=10042;
RN
    [1]
RP
    SEQUENCE FROM N.A.
RA
    Green R.M., Herbst M.M., Schountz T.;
RT
    "Cloning of the deer mouse tumor necrosis factor gene.";
    Submitted (MAR-2003) to the EMBL/GenBank/DDBJ databases.
RL
DR
    EMBL; AY249143; AAP03078.1; -.
    GO; GO:0016020; C:membrane; IEA.
DR
    GO; GO:0005164; F:tumor necrosis factor receptor binding; IEA.
DR
    GO; GO:0006955; P:immune response; IEA.
DR
DR
    InterPro; IPR006053; TNF abc.
DR
    InterPro; IPR006052; TNF family.
    InterPro; IPR008983; TNF like.
   InterPro; IPR003636; TNF subf.
DR
    Pfam; PF00229; TNF; 1.
DR
DR
   PRINTS; PR01234; TNECROSISFCT.
DR ProDom; PD002012; TNF subf; 1.
   SMART; SM00207; TNF; 1.
DR
```

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DR
    PROSITE; PS00251; TNF 1; 1.
DR
    PROSITE; PS50049; TNF 2; 1.
KW
    Signal.
FT
    SIGNAL
                 1
                      20
                              Potential.
FT
    CHAIN
                80
                    >232
                               tumor necrosis factor.
    NON TER
FT
               232
                    232
    SEQUENCE 232 AA; 25704 MW; E48A9379DB4F216D CRC64;
SO
                         8.2%; Score 137.5; DB 11; Length 232;
  Query Match
  Best Local Similarity 25.9%; Pred. No. 0.00036;
  Matches
          42; Conservative 27; Mismatches 58; Indels 35; Gaps
                                                                        7:
         163 QPFAHLTINATDIPSGSHKVSLS-SWYHDRGWAKISN-MTFSNGKLIVNQDGFYYLYANI 220
Qy
             90 KPVAHVVAN------HQVDEQLEWLSRRANALLANGMDLKDNQLVIPADGLYLVYSQV 141
Db
         221 CFRHHETSGDLATEYLQLMVYVTK-----TSIKIPSSHTLMKGGSTKYWSGNS 268
Qу
                  | : |: | |::
                                               ::|| :|
                                                             1 1
Db
         142 LFK-----GQGCSNYVLLTHTVSRFAVSYEDKVNLLSAIKSPCPKETPEGSELKPW---- 192
        269 EFHFYSINVGGFFKLRSGEEISIEVSNPSLLD-PDQDATYFG 309
Qy
               Db
         193 ---YEPIYLGGVFQLEKGDRLSAEVNLPKYLDFAESGQVYFG 231
RESULT 15
097543
ID
    097543
               PRELIMINARY; PRT; 149 AA.
    01-MAY-1999 (TrEMBLrel. 10, Created)
DT
    01-MAY-1999 (TrEMBLrel. 10, Last sequence update)
    01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
DT
DE
    Tumor necrosis factor alpha (Fragment).
GN
    TNF-ALPHA.
    Aotus nancymaae (Ma's night monkey).
OS
OC
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
    Mammalia; Eutheria; Primates; Platyrrhini; Cebidae; Aotinae; Aotus.
OC
OX
    NCBI TaxID=37293;
RN
    [1]
RP
    SEQUENCE FROM N.A.
RA
    Echeverry S.J., Hernandez E., Moreno A., Patarroyo M.E., Murillo L.A.;
    "Identification, cloning and sequencing of different interleukin genes
RT
RT
    in 4 Aotus species.";
    Submitted (JUL-1997) to the EMBL/GenBank/DDBJ databases.
RL
    EMBL; AF014513; AAD01539.1; -.
DR
    HSSP; P01375; 4TSV.
DR
DR
    GO; GO:0016020; C:membrane; IEA.
    GO; GO:0005164; F:tumor necrosis factor receptor binding; IEA.
DR
DR
    GO; GO:0006955; P:immune response; IEA.
DR
    InterPro; IPR006053; TNF abc.
    InterPro; IPR006052; TNF family.
    InterPro; IPR008983; TNF like.
DR
    InterPro; IPR003636; TNF subf.
DR
DR
    Pfam; PF00229; TNF; 1.
    PRINTS; PR01234; TNECROSISFCT.
DR
DR
    ProDom; PD002012; TNF subf; 1.
    SMART; SM00207; TNF; \overline{1}.
DR
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DR
   PROSITE; PS00251; TNF 1; 1.
   PROSITE; PS50049; TNF 2; 1.
DR
   FT
   NON_TER
FT
SQ
   SEQUENCE 149 AA; 16466 MW; 3C2A6140778EFA8A CRC64;
                    7.9%; Score 133; DB 6; Length 149;
 Query Match
 Best Local Similarity 25.5%; Pred. No. 0.00048;
 Matches 40; Conservative 31; Mismatches 62; Indels 24; Gaps
Qу
       163 QPFAHLTINATDIPSGSHKVSLSSWYHDRGWAKISN-MTFSNGKLIVNQDGFYYLYANIC 221
          4 KPVAHVVAN----PQAEGQL---QWLNRRANALLANGVELRDNQLVVPSEGLYLIYSQVL 56
Db
       222 FRHH--ETSGDLATEYLQLMV--YVTK----TSIKIPSSHTLMKGGSTKYWSGNSEFHFY 273
Qу
          57 FKGQGCPSTHVLLTHTISRIAVSYQTKVNLLSAIKSPCQRETPEGAEAKPW-----YE 109
Db
       274 SINVGGFFKLRSGEEISIEVSNPSLLD-PDQDATYFG 309
Qу
           110 PIYLGGVFOLEKGDRLSAEINRPDYLDFAESGQVYFG 146
Db
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Search completed: February 25, 2004, 16:30:28 Job time: 52 secs

GenCore version 5.1.6 Copyright (c) 1993 - 2004 Compugen Ltd.

OM protein - protein search, using sw model

Run on: February 25, 2004, 16:13:36; Search time 17 Seconds

(without alignments)

970.955 Million cell updates/sec

Title: US-09-787-126-2

Perfect score: 1685

Sequence: 1 MRRASRDYTKYLRGSEEMGG.....LLDPDQDATYFGAFKVRDID 317

Scoring table: BLOSUM62

Gapop 10.0 , Gapext 0.5

Searched: 141681 seqs, 52070155 residues

Total number of hits satisfying chosen parameters: 141681

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%

Maximum Match 100%

Listing first 45 summaries

Database : SwissProt_42:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

		용				
Result		Query				
No.	Score	Match	Length	DB	ID	Description
1	 1685	100.0	317	 1	TN11 HUMAN	014788 h tumor nec
2	1417.5	84.1	316	1	TN11 MOUSE	035235 m tumor nec
3	1396.5	82.9	318	1	TN11 RAT	Q9ese2 r tumor nec
4	251.5	14.9	281	1	TN10 HUMAN	P50591 homo sapien
5	248	14.7	291	1	TN10 MOUSE	P50592 mus musculu
6	200	11.9	282	1	TNF6 PIG	Q9bea8 sus scrofa
7	189	11.2	281	1	TNF6 HUMAN	P48023 homo sapien
8	186	11.0	280	1	TNF6 MACMU	Q9myl6 macaca mula
9	184.5	10.9	279	1	TNF6 MOUSE	P41047 mus musculu
10	182.5	10.8	280	1	TNF6 CERTO	Q9bdnl cercocebus
11	176.5	10.5	261	1	TNF5 BOVIN	P51749 bos taurus
12	175.5	10.4	278	1	TNF6 RAT	P36940 rattus norv
13	169.5	10.1	261	1	TNF5 CALJA	Q9bdn3 callithrix
14	167.5	9.9	261	1	TNF5 AOTTR	Q9bdm3 aotus trivi
15	158.5	9.4	261	1	TNF5 HUMAN	P29965 homo sapien
16	155.5	9.2	261	1	TNF5 MACMU	Q9bdc7 macaca mula
17	155	9.2	272	1	TNF5_CHICK	Q9i8d8 gallus gall

18	152.5	9.1	261	1	TNF5_PIG	Q95mq5	sus scrofa
19	152	9.0	260	1	TNF5_FELCA	097605	felis silve
20	146	8.7	234	1	TNFA_CAVPO	P51435	cavia porce
21	145.5	8.6	239	1	TN14 MOUSE	Q9qyh9	mus musculu
22	145	8.6	174	1	TN15 HUMAN	095150	homo sapien
23	145	8.6	260	1	TNF5_CANFA	097626	canis famil
24	143	8.5	240	1	TNF5 MACNE	Q9bdm7	macaca neme
25	141.5	8.4	235	1	TNFA MOUSE	P06804	mus musculu
26	140.5	8.3	235	1	TNFA RABIT	P04924	oryctolagus
27	139	8.2	233	1	TNFA SAISC	Q8mkg8	saimiri sci
28	137	8.1	234	1	TNFA SHEEP	P23383	ovis aries
29	136	8.1	234	1	TNFA CAPHI	P13296	capra hircu
30	134.5	8.0	310	1	TNFC_MARMO	Q9jm10	marmota mon
31	134	8.0	233	1	TNFA MACFA	P79337	macaca fasc
32	134	8.0	240	1	TN14_HUMAN	043557	homo sapien
33	133	7.9	232	1	TNFA_PANTR	Q8hzd9	pan troglod
34	133	7.9	233	1	TNFA_CANFA	P51742	canis famil
35	133	7.9	233	1	TNFA_HUMAN	P01375	homo sapien
36	133	7.9	233	1	TNFA MACMU	P48094	macaca mula
37	132.5	7.9	235	1	TNFA_PERLE	P36939	peromyscus
38	131.5	7.8	235	1	TNFA_RAT	P16599	rattus norv
39	130.5	7.7	306	1	TNFC_MOUSE	P41155	mus musculu
40	130	7.7	233	1	TNFA_PAPSP	P33620	papio sp. (
41	129.5	7.7	233	1	TNFA_MARMO	035734	marmota mon
42	129	7.7	233	1	TNFA_PAPAN		papio anubi
43	129	7.7	233	1	TNFA_PAPHU		papio hamad
44	128	7.6	234	1	TNFA_HORSE		equus cabal
45	126.5	7.5	233	1	TNFA_BOVIN	Q06599	bos taurus

ALIGNMENTS

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RESULT 1
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                                          317 AA.
                   STANDARD;
ID
     TN11 HUMAN
     014788; 014723; Q96Q17; Q9P2Q3;
AC
     16-OCT-2001 (Rel. 40, Created)
DT
     16-OCT-2001 (Rel. 40, Last sequence update)
DT
     10-OCT-2003 (Rel. 42, Last annotation update)
DT
     Tumor necrosis factor ligand superfamily member 11 (Receptor activator
DE
     of nuclear factor kappa B ligand) (RANKL) (TNF-related activation-
DE
     induced cytokine) (TRANCE) (Osteoprotegerin ligand) (OPGL) (Osteoclast
DΕ
DE
     differentiation factor) (ODF).
     TNFSF11 OR RANKL OR TRANCE OR OPGL.
GN
     Homo sapiens (Human).
OS
     Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
     Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OC
     NCBI TaxID=9606;
OX
RN
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     SEQUENCE FROM N.A. (ISOFORM 1).
RP
     TISSUE=Bone marrow, and Peripheral blood;
RC
     MEDLINE=98032977; PubMed=9367155;
RX
     Anderson D.M., Maraskovsky E., Billingsley W.L., Dougall W.C.,
RA
     Tometsko M.E., Roux E.R., Teepe M.C., DuBose R.F., Cosman D.,
RA
RA
     Galibert L.;
     "A homologue of the TNF receptor and its ligand enhance T-cell growth
RT
```

```
RT
     and dendritic-cell function.";
RL
    Nature 390:175-179(1997).
RN
     SEQUENCE FROM N.A. (ISOFORM 1).
RP
     TISSUE=Lymph node;
RC
     MEDLINE=98227661; PubMed=9568710;
RX
     Lacey D.L., Timms E., Tan H.-L., Kelley M.J., Dunstan C.R.,
RA
     Burgess T., Elliott R., Colombero A., Elliott G., Scully S., Hsu H.,
RA
     Sullivan J., Hawkins N., Davy E., Capparelli C., Eli A., Qian Y.-X.,
RA
     Kaufman S., Sarosi I., Shalhoub V., Senaldi G., Guo J., Delaney J.,
RA
RA
     Boyle W.J.;
     "Osteoprotegerin ligand is a cytokine that regulates osteoclast
RT
     differentiation and activation.";
RT
     Cell 93:165-176(1998).
RL
RN
     [3]
     SEQUENCE FROM N.A. (ISOFORMS 1; 2 AND 3).
RΡ
RA
     Ikeda T., Kuroyama H., Hirokawa K.;
     "Determination of human RANKL isoforms.";
RT
     Submitted (JUN-2001) to the EMBL/GenBank/DDBJ databases.
RL
RN
RP
     SEQUENCE OF 73-317 FROM N.A.
RC
     TISSUE=Thymocytes;
     MEDLINE=97460112; PubMed=9312132;
RX
     Wong B.R., Rho J., Arron J., Robinson E., Orlinick J., Chao M.,
RA
     Kalachikov S., Cayani E., Bartlett F.S. III, Frankel W.N., Lee S.Y.,
RA
     Choi Y.;
RA
     "TRANCE is a novel ligand of the tumor necrosis factor receptor family
RT
     that activates c-Jun N-terminal kinase in T cells.";
RT
     J. Biol. Chem. 272:25190-25194(1997).
RL
RN
     SEQUENCE FROM N.A. (ISOFORM 2).
RP
RC
     TISSUE=Tonque;
     MEDLINE=20175237; PubMed=10708588;
RX
     Nagai M., Kyakumoto S., Sato N.;
RA
     "Cancer cells responsible for humoral hypercalcemia express mRNA
RT
RT
     encoding a secreted form of ODF/TRANCE that induces osteoclast
RT
     formation.";
     Biochem. Biophys. Res. Commun. 269:532-536(2000).
RL
     -!- FUNCTION: Cytokine that binds to TNFRSF11B/OPG and to
CC
         TNFRSF11A/RANK. Osteoclast differentiation and activation factor.
CC
         Augments the ability of dendritic cells to stimulate naive T-cell
CC
         proliferation. May be an important regulator of interactions
CC
         between T cells and dendritic cells and may play a role in the
CC
         regulation of the T cell-dependent immune response. May also play
CC
         an important role in enhanced bone-resorption in humoral
CC
CC
         hypercalcemia of malignancy.
     -!- SUBUNIT: Homotrimer (By similarity).
CC
     -!- SUBCELLULAR LOCATION: Type II membrane protein (isoforms 1 and 3);
CC
         Secreted (isoform 2). A soluble form of isoform 1 arises by
CC
CC
         proteolytic processing (By similarity).
CC
     -!- ALTERNATIVE PRODUCTS:
         Event=Alternative splicing; Named isoforms=3;
CC
CC
CC
           IsoId=014788-1; Sequence=Displayed;
CC
         Name=2; Synonyms=SODF;
CC
           IsoId=014788-2; Sequence=VSP 006447;
CC
         Name=3;
```

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CC
          IsoId=014788-3; Sequence=VSP 006446;
    -!- TISSUE SPECIFICITY: HIGHEST IN THE PERIPHERAL LYMPH NODES BUT WEAK
CC
        IN SPLEEN, PERIPHERAL BLOOD LEUKOCYTES, BONE MARROW, HEART,
CC
        PLACENTA, SKELETAL MUSCLE, STOMACH AND THYROID.
CC
    -!- INDUCTION: UPREGULATED BY T CELL RECEPTOR STIMULATION.
CC
    -!- PTM: The soluble form of isoform 1 derives from the membrane form
CC
        by proteolytic processing (By similarity). The cleavage may be
CC
CC
        catalyzed by ADAM17.
    -!- SIMILARITY: Belongs to the tumor necrosis factor family.
CC
    _____
CC
    This SWISS-PROT entry is copyright. It is produced through a collaboration
CC
    between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC
    the European Bioinformatics Institute. There are no restrictions on its
CC
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    modified and this statement is not removed. Usage by and for commercial
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    entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC
CC
    or send an email to license@isb-sib.ch).
CC
    EMBL; AF019047; AAB86811.1; -.
DR
    EMBL; AF053712; AAC39731.1; -.
DR
    EMBL; AB064269; BAB79694.1; -.
DR
    EMBL; AB061227; BAB71768.1; -.
DR
DR
    EMBL; AB064270; BAB79695.1; -.
    EMBL; AF013171; AAC51762.1; -.
DR
    EMBL; AB037599; BAA90488.1; -.
DR
    HSSP; P50591; 1D0G.
DR
    Genew; HGNC:11926; TNFSF11.
DR
DR
    MIM; 602642; -.
    GO; GO:0005576; C:extracellular; NAS.
DR
    GO; GO:0005887; C:integral to plasma membrane; NAS.
DR
    GO; GO:0005164; F:tumor necrosis factor receptor binding; NAS.
    GO; GO:0006955; P:immune response; NAS.
DR
    GO; GO:0030316; P:osteoclast differentiation; NAS.
DR
    InterPro; IPR006052; TNF family.
DR
    InterPro; IPR008983; TNF like.
DR
    InterPro; IPR003636; TNF subf.
DR
DR
    Pfam; PF00229; TNF; 1.
    ProDom; PD002012; TNF subf; 1.
DR
    SMART; SM00207; TNF; 1.
DR
    PROSITE; PS00251; TNF 1; FALSE NEG.
DR
    PROSITE; PS50049; TNF 2; 1.
DR
    Cytokine; Differentiation; Receptor; Glycoprotein; Transmembrane;
    Signal-anchor; Alternative splicing.
KW
                       317
                                TUMOR NECROSIS FACTOR LIGAND SUPERFAMILY
FT
    CHAIN
                1
                                MEMBER 11, MEMBRANE FORM.
FT
                                TUMOR NECROSIS FACTOR LIGAND SUPERFAMILY
FT
    CHAIN
                140
                       317
                                MEMBER 11, SOLUBLE FORM (BY SIMILARITY).
FT
                 1
                       47
                                CYTOPLASMIC (POTENTIAL).
    DOMAIN
FT
                                SIGNAL-ANCHOR (TYPE-II MEMBRANE PROTEIN)
FT
    TRANSMEM
                 48
                       68
FT
                                (POTENTIAL).
                69 317
                                EXTRACELLULAR (POTENTIAL).
FT
    DOMAIN
               139 140
                               CLEAVAGE (BY SIMILARITY).
FT
    SITE
    CARBOHYD 171
                     171
                                N-LINKED (GLCNAC. . .) (POTENTIAL).
FΤ
              198 198
                               N-LINKED (GLCNAC. . .) (POTENTIAL).
FT
    CARBOHYD
                       47
                               Missing (in isoform 3).
FT
    VARSPLIC
                1
FT
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FT
    VARSPLIC 1 73
                               Missing (in isoform 2).
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FT
                             A \rightarrow G (IN REF. 4).
             194 194
FT
    CONFLICT
             317 AA; 35478 MW; 766176446348097F CRC64;
SO
    SEOUENCE
                      100.0%; Score 1685; DB 1; Length 317;
 Query Match
                     100.0%; Pred. No. 3.6e-138;
 Best Local Similarity
                          0; Mismatches
                                            0; Indels
                                                        0; Gaps
                                                                   0;
 Matches 317; Conservative
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Qу
            1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
Db
         61 VCSVALFFYFRAOMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
Qу
            61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
Db
        121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
Qу
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Db
        181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
QУ
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Db
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QУ
            241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Db
        301 PDQDATYFGAFKVRDID 317
QУ
            Db
        301 PDODATYFGAFKVRDID 317
RESULT 2
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ID
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                 STANDARD;
                              PRT;
    035235; 035306; Q9JJK8; Q9JJK9; Q9R1Y0;
AC
DT
    16-OCT-2001 (Rel. 40, Created)
    16-OCT-2001 (Rel. 40, Last sequence update)
DT
    10-OCT-2003 (Rel. 42, Last annotation update)
DT
    Tumor necrosis factor ligand superfamily member 11 (Receptor activator
DE
    of nuclear factor kappa B ligand) (RANKL) (TNF-related activation-
DΕ
    induced cytokine) (TRANCE) (Osteoprotegerin ligand) (OPGL) (Osteoclast
DΕ
    differentiation factor) (ODF) (Osteoclastogenesis-inhibitory factor)
DF.
DE
GN
    TNFSF11 OR RANKL OR TRANCE OR OPGL.
    Mus musculus (Mouse).
OS
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OC
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    Wong B.R., Rho J., Arron J., Robinson E., Orlinick J., Chao M.,
RA
    Kalachikov S., Cayani E., Bartlett F.S. III, Frankel W.N., Lee S.Y.,
RA
RA
    Choi Y.;
```

```
"TRANCE is a novel ligand of the tumor necrosis factor receptor family
RT
     that activates c-Jun N-terminal kinase in T cells.";
RT
     J. Biol. Chem. 272:25190-25194(1997).
RL
RN
     SEQUENCE FROM N.A. (ISOFORM 1).
RP
RC
     TISSUE=Thymic lymphoma;
    MEDLINE=98032977; PubMed=9367155;
RX
     Anderson D.M., Maraskovsky E., Billingsley W.L., Dougall W.C.,
RA
     Tometsko M.E., Roux E.R., Teepe M.C., DuBose R.F., Cosman D.,
RA
RA
     Galibert L.;
     "A homologue of the TNF receptor and its ligand enhance T-cell growth
RT
     and dendritic-cell function.";
RT
     Nature 390:175-179(1997).
RL
RN
     SEQUENCE FROM N.A. (ISOFORM 1).
RP
     TISSUE=Bone marrow;
RC
     MEDLINE=98227661; PubMed=9568710;
RX
     Lacey D.L., Timms E., Tan H.-L., Kelley M.J., Dunstan C.R.,
RA
     Burgess T., Elliott R., Colombero A., Elliott G., Scully S., Hsu H.,
RA
     Sullivan J., Hawkins N., Davy E., Capparelli C., Eli A., Qian Y.-X.,
RA
     Kaufman S., Sarosi I., Shalhoub V., Senaldi G., Guo J., Delaney J.,
RA
RA
     Boyle W.J.;
     "Osteoprotegerin ligand is a cytokine that regulates osteoclast
RT
     differentiation and activation.";
RT
     Cell 93:165-176(1998).
RL
RN
     [4]
     SEQUENCE FROM N.A. (ISOFORM 1).
RP
     TISSUE=Bone marrow stroma;
RC
     MEDLINE=98188248; PubMed=9520411;
RX
     Yasuda H., Shima N., Nakagawa N., Yamaguchi K., Kinosaki M.,
RA.
     Mochizuki S.-I., Tomoyasu A., Yano K., Goto M., Murakami A., Tsuda E.,
     Morinaga T., Higashio K., Udagawa N., Takahashi N., Suda T.;
RA
     "Osteoclast differentiation factor is a ligand for
RT
     osteoprotegerin/osteoclastogenesis-inhibitory factor and is identical
RT
RT
     to TRANCE/RANKL.";
     Proc. Natl. Acad. Sci. U.S.A. 95:3597-3602(1998).
RL
RN
RP
     SEQUENCE FROM N.A. (ISOFORM 1).
RC
     STRAIN=129;
     MEDLINE=99214075; PubMed=10196481;
RX
     Kodaira K., Kodaira K., Mizuno A., Yasuda H., Shima N., Murakami A.,
RA
RA
     Ueda M., Higashio K.;
     "Cloning and characterization of the gene encoding mouse osteoclast
RT
RT
     differentiation factor.";
     Gene 230:121-127(1999).
RL
RN
     [6]
     SEQUENCE FROM N.A. (ISOFORMS 1; 2 AND 3).
RP
     MEDLINE=21150053; PubMed=11250921;
RX
     Ikeda T., Kasai M., Utsuyama M., Hirokawa K.;
RA
     "Determination of three isoforms of the receptor activator of nuclear
RТ
     factor-kappaB ligand and their differential expression in bone and
RT
RT
     thymus.";
     Endocrinology 142:1419-1426(2001).
RL
RN
     SEQUENCE OF 139-147, PROCESSING, AND N-GLYCOSYLATION.
RP
     MEDLINE=99240759; PubMed=10224132;
RX
     Lum L., Wong B.R., Josien R., Becherer J.D., Erdjument-Bromage H.,
RA
```

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Schloendorff J., Tempst P., Choi Y., Blobel C.P.;
RA
     "Evidence for a role of a tumor necrosis factor-alpha
RT
     (TNF-alpha)-converting enzyme-like protease in shedding of TRANCE, a
RT
    TNF family member involved in osteoclastogenesis and dendritic cell
RT
     survival.";
RT
     J. Biol. Chem. 274:13613-13618(1999).
RL
RN
    X-RAY CRYSTALLOGRAPHY (2.6 ANGSTROMS) OF 158-316.
RP
    MEDLINE=21464816; PubMed=11581298;
RX
    Lam J., Nelson C.A., Ross F.P., Teitelbaum S.L., Fremont D.H.;
     "Crystal structure of the TRANCE/RANKL cytokine reveals determinants
RT
     of receptor-ligand specificity.";
RT
     J. Clin. Invest. 108:971-979(2001).
RL
RN
    [9]
    X-RAY CRYSTALLOGRAPHY (2.2 ANGSTROMS) OF 137-316.
RP
    MEDLINE=21839021; PubMed=11733492;
RX
    Ito S., Wakabayashi K., Ubukata O., Hayashi S., Okada F., Hata T.;
     "Crystal structure of the extracellular domain of mouse RANK ligand at
RT
RT
     2.2-A resolution.";
    J. Biol. Chem. 277:6631-6636(2002).
RL
    -!- FUNCTION: Cytokine that binds to TNFRSF11B/OPG and to
CC
CC
         TNFRSF11A/RANK. Osteoclast differentiation and activation factor.
         Augments the ability of dendritic cells to stimulate naive T-cell
CC
         proliferation. May be an important regulator of interactions
CC
         between T cells and dendritic cells and may play a role in the
CC
         regulation of the T cell-dependent immune response. May also play
CC
         an important role in enhanced bone-resorption in humoral
CC
CC
         hypercalcemia of malignancy.
CC
     -!- SUBUNIT: Homotrimer.
    -!- SUBCELLULAR LOCATION: Type II membrane protein and secreted
CC
         (isoforms 1 and 2); Cytoplasmic (isoform 3).
CC
CC
     -!- ALTERNATIVE PRODUCTS:
         Event=Alternative splicing; Named isoforms=3;
CC
CC
         Name=1;
           IsoId=035235-1; Sequence=Displayed;
CC
CC
         Name=2:
           IsoId=035235-2; Sequence=VSP 006449;
CC
CC
         Name=3;
CC
           IsoId=035235-3; Sequence=VSP 006448;
     -!- TISSUE SPECIFICITY: HIGHLY EXPRESSED IN THYMUS AND LYMPH NODES BUT
CC
         NOT IN NONLYMPHOID TISSUES AND IS ABUNDANTLY EXPRESSED IN T CELLS
CC
         BUT NOT IN B CELLS. A HIGH LEVEL EXPRESSION IS ALSO SEEN IN THE
CC
CC
         TRABECULAR BONE AND LUNG.
     -!- PTM: N-glycosylated.
CC
     -!- PTM: The soluble form of isoform 1 derives from the membrane form
CC
         by proteolytic processing. The cleavage may be catalyzed by
CC
         ADAM17. A further shorter soluble form was observed.
CC
     -!- DISEASE: Deficiency in TNFSF11 results in failure to form lobulo-
CC
         alveolar mammary structures during pregnancy, resulting in death
CC
         of newborns. Trance-deficient mice show severe osteopetrosis, with
CC
         no osteoclasts, marrow spaces, or tooth eruption, and exhibit
CC
         profound growth retardation at several skeletal sites, including
CC
         the limbs, skull, and vertebrae and have marked chondrodysplasia,
CC
         with thick, irregular growth plates and a relative increase in
CC
         hypertrophic chondrocytes.
CC
CC
     -!- SIMILARITY: Belongs to the tumor necrosis factor family.
```

```
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    between the Swiss Institute of Bioinformatics and the EMBL outstation -
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    the European Bioinformatics Institute. There are no restrictions on its
CC
    use by non-profit institutions as long as its content is in no way
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CC
    modified and this statement is not removed. Usage by and for commercial
    entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC
CC
    or send an email to license@isb-sib.ch).
    CC
    EMBL; AF013170; AAC71061.1; -.
DR
    EMBL; AF019048; AAB86812.1; -.
DR
    EMBL; AF053713; AAC40113.1; -.
DR
    EMBL; AB008426; BAA25425.1; -.
DR
    EMBL; AB022039; BAA36970.1; -.
DR
    EMBL; AB022036; BAA36970.1; JOINED.
DR
DR
    EMBL; AB022037; BAA36970.1; JOINED.
    EMBL; AB022038; BAA36970.1; JOINED.
DR
    EMBL; AB032771; BAA97257.1; -.
    EMBL; AB032772; BAA97258.1; -.
DR
    EMBL; AB036798; BAA97259.1; -.
DR
    PDB; 1JTZ; 28-JAN-03.
DR
    PDB; 1IQA; 14-JAN-03.
DR
DR
    MGD; MGI:1100089; Tnfsf11.
DR
    GO; GO:0009887; P:organogenesis; IMP.
DR
    GO; GO:0001503; P:ossification; IMP.
    InterPro; IPR006052; TNF family.
DR
    InterPro; IPR008983; TNF like.
DR
    InterPro; IPR003636; TNF subf.
DR
DR
    Pfam; PF00229; TNF; 1.
    ProDom; PD002012; TNF subf; 1.
DR
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DR
    PROSITE; PS00251; TNF 1; FALSE NEG.
DR
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    Cytokine; Differentiation; Receptor; Glycoprotein; Transmembrane;
KW
    Signal-anchor; 3D-structure; Alternative splicing.
KW
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                     316
FT
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                  1
FT
                                MEMBER 11, MEMBRANE FORM.
                                TUMOR NECROSIS FACTOR LIGAND SUPERFAMILY
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    CHAIN
           139
                       316
                                MEMBER 11, SOLUBLE FORM.
FT
                                CYTOPLASMIC (POTENTIAL).
FT
    DOMAIN
                     48
FT
    TRANSMEM
                49
                       69
                                SIGNAL-ANCHOR (TYPE-II MEMBRANE PROTEIN)
FT
                                (POTENTIAL).
                70
                       316
                                EXTRACELLULAR (POTENTIAL).
FT
    DOMAIN
                    139
197
262
FT
    SITE
                138
                                CLEAVAGE.
               197
                                N-LINKED (GLCNAC. . .) (POTENTIAL).
FT
    CARBOHYD
             262
                                N-LINKED (GLCNAC. . .) (POTENTIAL).
FT
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                    117
                                Missing (in isoform 3).
FT
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                1
                                /FTId=VSP 006448.
FT
              14
    VARSPLIC
                       44
                                SSEEMGSGPGVPHEGPLHPAPSAPAPAPPPA -> TP (in
FT
FT
                                isoform 2).
FT
                                /FTId=VSP 006449.
               99
                       99
                                G \rightarrow D (IN REF. 2).
FT
    CONFLICT
                141
                                MISSING (IN REF. 5).
FT
    CONFLICT
                       143
FT
    STRAND
               164
                     169
FT
    TURN
                171
                     172
FT
    STRAND
                181
                      182
FT
    STRAND
                186
                       187
FT
    TURN
                191
                       192
```

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FΤ
         STRAND
                               194
                                            196
FT
         STRAND
                               198
                                            201
FT
         TURN
                               202
                                            203
FT
         STRAND
                               204
                                            207
                                            224
                               211
FT
         STRAND
                                            227
FT
         HELIX
                               225
         STRAND
                               234
                                            245
FT
                                                84.1%; Score 1417.5; DB 1; Length 316;
   Ouerv Match
   Best Local Similarity
                                             84.3%; Pred. No. 4.7e-115;
                                                                                                                                              2;
   Matches 268; Conservative 16; Mismatches
                                                                                                     Indels
                                                                                                                               Gaps
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Db
                    60 VVCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRI 119
Qу
                          61 VVCSIALFLYFRAQMDPNRISEDSTHCFYRILRLHENAGLQDSTLESEDT--LPDSCRRM 118
Db
                  120 KQAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGS 179
Qу
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Db
                  180 HKVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLM 239
Qу
                          179 HKVTLSSWYHDRGWAKISNMTLSNGKLRVNQDGFYYLYANICFRHHETSGSVPTDYLQLM 238
Db
                  240 VYVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLL 299
Qу
                          11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11
                  239 VYVVKTSIKIPSSHNLMKGGSTKNWSGNSEFHFYSINVGGFFKLRAGEEISIQVSNPSLL 298
Db
                  300 DPDQDATYFGAFKVRDID 317
QУ
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Db
                  299 DPDODATYFGAFKVQDID 316
RESULT 3
TN11 RAT
                                     STANDARD;
                                                                 PRT:
                                                                             318 AA.
         TN11 RAT
ID
         Q9ESE2; Q91ZI9;
AC
         28-FEB-2003 (Rel. 41, Created)
DT
         28-FEB-2003 (Rel. 41, Last sequence update)
DT
         28-FEB-2003 (Rel. 41, Last annotation update)
DT
         Tumor necrosis factor ligand superfamily member 11 (Receptor activator
         of nuclear factor kappa B ligand) (RANKL) (TNF-related activation-
DΕ
         induced cytokine) (TRANCE) (Osteoprotegerin ligand) (OPGL) (Osteoclast
DΕ
         differentiation factor) (ODF).
DΕ
         TNFSF11 OR RANKL OR TRANCE OR OPGL.
GN
         Rattus norvegicus (Rat).
OS
         Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
         Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
OC
         NCBI TaxID=10116;
OX
RN
         [1]
RP
         SEQUENCE FROM N.A.
         TISSUE=Tibial bone;
RC
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RX
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Xu J.K., Tan J.K., Huang L., Gao X.H., Laird R., Liu D., Wysocki S.,
RA
RA
    Zheng M.H.;
    "Cloning, sequence and functional characterization of the rat
RT
    homologue of receptor activator of NF-kB ligand.";
RT
    J. Bone Miner. Res. 15:2178-2186(2000).
RL
RN
    SEQUENCE OF 266-318 FROM N.A.
RP
RC
    STRAIN=Fischer 344;
    MEDLINE=21662371; PubMed=11804028;
RX
    Odgren P.R., Kim N., van Wesenbeeck L., MacKay C., Mason-Savas A.,
RA
    Safadi F.F., Popoff S.N., Lengner C., van-Hul W., Choi Y.,
RA
RA
    Marks S.C. Jr.;
    "Evidence that the rat osteopetrotic mutation toothless (tl) is not in
RT
    the TNFSF11 (TRANCE, RANKL, ODF, OPGL) gene.";
RT
RL
    Int. J. Dev. Biol. 45:853-859(2001).
    -!- FUNCTION: Cytokine that binds to TNFRSF11B/OPG and to
CC
        TNFRSF11A/RANK. Osteoclast differentiation and activation factor.
CC
        Augments the ability of dendritic cells to stimulate naive T-cell
CC
        proliferation. May be an important regulator of interactions
CC
        between T cells and dendritic cells and may play a role in the
CC
        regulation of the T cell-dependent immune response. May also play
CC
CC
        an important role in enhanced bone-resorption in humoral
CC
        hypercalcemia of malignancy.
CC
    -!- SUBUNIT: Homotrimer (By similarity).
    -!- SUBCELLULAR LOCATION: Type II membrane protein and secreted (By
CC
CC
        similarity).
    -!- TISSUE SPECIFICITY: Highly expressed in thymus and bone tissues.
CC
    -!- PTM: The soluble form derives from the membrane form by
CC
        proteolytic processing (By similarity).
CC
    -!- SIMILARITY: Belongs to the tumor necrosis factor family.
CC
    ______
CC
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    or send an email to license@isb-sib.ch).
     _____
CC
    EMBL; AF187319; AAG17031.1; -.
DR
     EMBL; AF425669; AAL23963.1; -.
DR
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DR
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     InterPro; IPR003636; TNF subf.
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DR
     ProDom; PD002012; TNF subf; 1.
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     Cytokine; Differentiation; Receptor; Glycoprotein; Transmembrane;
KW
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ΚW
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     CHAIN
                  1
                       318
FT
                                MEMBER 11, MEMBRANE FORM.
FT
                       318
                                TUMOR NECROSIS FACTOR LIGAND SUPERFAMILY
FT
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                141
                                MEMBER 11, SOLUBLE FORM.
FT
                      47
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                 1
FT
     DOMAIN
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FT
              48
                    68
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    TRANSMEM
                             (POTENTIAL).
FT
              69
                  318
                             EXTRACELLULAR (POTENTIAL).
FT
    DOMAIN
                  141
                             CLEAVAGE (BY SIMILARITY).
FT
    SITE
              140
                             N-LINKED (GLCNAC. . .) (POTENTIAL).
                   199
              199
FT
    CARBOHYD
                             N-LINKED (GLCNAC. . .) (POTENTIAL).
              264
                    264
FT
    CARBOHYD
                             I \rightarrow M (IN REF. 2).
             317
                   317
FT
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SQ
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 Best Local Similarity 82.4%; Pred. No. 3.1e-113;
 Matches 262: Conservative 19; Mismatches 36; Indels
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                                                        1; Gaps
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Qу
            1 MRRANRDYGKYLRGSEEMGSCPGVPHEGPLHPAPSAPAPAPPPAASRFMFLALLGLGLGQ 60
Db
         60 VVCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRI 119
Qу
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Db
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Qу
            121 KQAFQGAVQRELQHIVGPQRFSGVPAMMEGSWLDVARRGKPEAQPFAHLTINAADIPSGS 180
Dh
        180 HKVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLM 239
QУ
            181 HKVSLSSWYHDRGWAKISNMTLSNGKLRVNQDGFYYLYANICFRHHETSGSVPADYLQLM 240
Db
        240 VYVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLL 299
Qу
            241 VYVVKTSIKIPSSHNLMKGGSTKNWSGNSEFHFYSINVGGFFKLRAGEEISVQVSNPSLL 300
Db
Qy
        300 DPDQDATYFGAFKVRDID 317
            Db
        301 DPDQDATYFGAFKVQDID 318
RESULT 4
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AC
    P50591;
    01-OCT-1996 (Rel. 34, Created)
DT
    01-OCT-1996 (Rel. 34, Last sequence update)
DT
    10-OCT-2003 (Rel. 42, Last annotation update)
    Tumor necrosis factor liqand superfamily member 10 (TNF-related
DE.
    apoptosis inducing ligand) (TRAIL protein) (Apo-2 ligand) (Apo-2L).
DE
    TNFSF10 OR TRAIL OR APO2L.
GN
    Homo sapiens (Human).
OS
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
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OX
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RN
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RP
    MEDLINE=96111955; PubMed=8777713;
RX
    Wiley S.R., Schooley K., Smolak P.J., Din W.S., Huang C.-P.,
RA
    Nicholl J.K., Sutherland G.R., Davis-Smith T., Rauch C., Smith C.A.,
RA
```

```
RA
     Goodwin R.G.;
     "Identification and characterization of a new member of the TNF
RT
RT
     family that induces apoptosis.";
RL
     Immunity 3:673-682(1995).
RN
     [2]
RP
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RC
     TISSUE=Placenta;
RX
     MEDLINE=96278649; PubMed=8663110;
RA
     Pitti R.M., Marsters S.A., Ruppert S., Donahue C.J., Moore A.,
RA
     Ashkenazi A.;
     "Induction of apoptosis by Apo-2 ligand, a new member of the tumor
RT
     necrosis factor cytokine family.";
RT
     J. Biol. Chem. 271:12687-12690(1996).
RL
RN
     [3]
     SEQUENCE FROM N.A.
RP
RC
     TISSUE=Lymph;
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     MEDLINE=22388257; PubMed=12477932;
RA
     Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
     Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
RA
     Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
RA
     Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
RA
     Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
RA
     Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,
RA
     Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
RA
     Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
RA
     Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
RA
     Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
RA
     Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
RA
RA
     Fahey J., Helton E., Ketteman M., Madan A., Rodrigues S., Sanchez A.,
RA
     Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
RA
     Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,
     Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,
RA
     Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,
RA
     Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;
RA
RT
     "Generation and initial analysis of more than 15,000 full-length
RT
     human and mouse cDNA sequences.";
RL
     Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
RN
RP
     X-RAY CRYSTALLOGRAPHY (2.4 ANGSTROMS) OF 114-281.
RX
     MEDLINE=20017054; PubMed=10549288;
     Hymowitz S.G., Christinger H.W., Fuh G., Ultsch M., O'Connell M.,
RA
RA
     Kelley R.F., Ashkenazi A., de Vos A.M.;
RT
     "Triggering cell death: the crystal structure of Apo2L/TRAIL in a
     complex with death receptor 5.";
RT
RL
     Mol. Cell 4:563-571(1999).
RN
     X-RAY CRYSTALLOGRAPHY (2.2 ANGSTROMS) OF 119-281.
RP
RX
     PubMed=10542098;
RA
     Mongkolsapaya J., Grimes J.M., Chen N., Xu X.-N., Stuart D.I.,
RA
     Jones E.Y., Screaton G.R.;
RT
     "Structure of the TRAIL-DR5 complex reveals mechanisms conferring
     specificity in apoptotic initiation.";
RT
     Nat. Struct. Biol. 6:1048-1053(1999).
RL
RN
RP
     X-RAY CRYSTALLOGRAPHY (2.8 ANGSTROMS) OF 114-281.
RX
     MEDLINE=99413670; PubMed=10485660;
RA
     Cha S.-S., Kim M.S., Choi Y.H., Sung B.J., Shin N.K., Shin H.C.,
```

```
RA
    Sung Y.C., Oh B.-H.;
RT
    "2.8 A resolution crystal structure of human TRAIL, a cytokine with
RT
    selective antitumor activity.";
    Immunity 11:253-261(1999).
RL
CC
    -!- FUNCTION: Cytokine that binds to TNFRSF10A/TRAILR1,
        TNFRSF10B/TRAILR2, TNFRSF10C/TRAILR3, TNFRSF10D/TRAILR4 and
CC
        possibly also to TNFRSF11B/OPG. Induces apoptosis. Its activity
CC
CC
        may be modulated by binding to the decoy receptors
        TNFRSF10C/TRAILR3, TNFRSF10D/TRAILR4 and TNFRSF11B/OPG that cannot
CC
CÇ
        induce apoptosis.
    -!- COFACTOR: Binds 1 zinc ion and one anionic solvent molecule per
CC
CC
        trimer.
    -!- SUBUNIT: Homotrimer.
CC
    -!- SUBCELLULAR LOCATION: Type II membrane protein (Potential).
CC
    -!- TISSUE SPECIFICITY: WIDESPREAD; MOST PREDOMINANT IN SPLEEN, LUNG
CC
CC
       AND PROSTATE.
    -!- SIMILARITY: Belongs to the tumor necrosis factor family.
CC
    ______
CC
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CC
CC
    or send an email to license@isb-sib.ch).
    CC
    EMBL; U37518; AAC50332.1; -.
DR
    EMBL; U57059; AAB01233.1; -.
DR
    EMBL; BC032722; AAH32722.1; -.
DR
    PDB; 1D0G; 22-OCT-99.
DR
    PDB; 1D4V; 01-NOV-99.
DR
    PDB; 1D2Q; 11-FEB-00.
    PDB: 1DG6: 26-SEP-01.
DR
    Genew; HGNC:11925; TNFSF10.
DR
    MIM; 603598; -.
DR
    GO; GO:0005887; C:integral to plasma membrane; TAS.
DR
    GO; GO:0005625; C:soluble fraction; TAS.
DR
    GO; GO:0005102; F:receptor binding; TAS.
DR
DR
    GO; GO:0007267; P:cell-cell signaling; TAS.
    GO; GO:0006917; P:induction of apoptosis; TAS.
DR
    GO; GO:0007165; P:signal transduction; TAS.
    InterPro; IPR006052; TNF family.
DR
    InterPro; IPR008983; TNF like.
DR
    InterPro; IPR003636; TNF subf.
DR
DR
    Pfam; PF00229; TNF; 1.
    ProDom; PD002012; TNF subf; 1.
DR
    SMART; SM00207; TNF; 1.
    PROSITE; PS00251; TNF 1; 1.
DR
    PROSITE; PS50049; TNF 2; 1.
DR
    Cytokine; Apoptosis; Transmembrane; Signal-anchor; Metal-binding;
KW
    Zinc; 3D-structure.
KW
FT
    DOMAIN
              1 17
                               CYTOPLASMIC (POTENTIAL).
FT
    TRANSMEM
                18
                      38
                               SIGNAL-ANCHOR (TYPE-II MEMBRANE PROTEIN)
FT
                               (POTENTIAL).
FT
    DOMAIN
               39 281
                               EXTRACELLULAR (POTENTIAL).
FT
    METAL
               230
                      230
                               ZINC.
               123 127
    STRAND
FT
```

```
131
FT
     TURN
                 130
                137
FT
     TURN
                          139

      STRAND
      149

      STRAND
      163

      STRAND
      167

      TURN
      171

FT
                         150
FT
                        165
FT
                        170

    TURN
    171
    172

    STRAND
    173
    176

    STRAND
    180
    193

    STRAND
    205
    213

    STRAND
    220
    228

    STRAND
    237
    250

    TURN
    252
    253

    STRAND
    255
    260

    HELIX
    263
    265

    STRAND
    266
    267

    TURN
    270
    272

    STRAND
    274
    281

FT
     STRAND
FT
                 274 281
SQ SEQUENCE 281 AA; 32509 MW; DDAAAF78DAAB2F6D CRC64;
  Ouerv Match
                 14.9%; Score 251.5; DB 1; Length 281;
  Best Local Similarity 24.1%; Pred. No. 2.3e-14;
  Matches 71; Conservative 61; Mismatches 117; Indels 45; Gaps 10;
Qу
           42 PAASRSMFVALLGLGLGQVVCSVALFFYFRAQMD--PNRISEDGTHCIYRILRLHENADF 99
              Db
           10 PSLGQTCVLIVIFTVLLQSLCVAVTYVYFTNELKQMQDKYSKSGIACF-----LKED--- 61
Qу
         100 QDTTLESQDTKLIPDSCRRIKQAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSK 159
               Db
           62 -DSYWDPNDEESMNSPCWQVKW-----QLRQLVRKMILRTSEETI----STVOEKO 107
          160 LEAQPF-----AHLT----INATDIPSGSHKVSL---SSWYHDR-GWAKISNM 199
Qу
                  Db
          108 QNISPLVRERGPQRVAAHITGTRGRSNTLSSPNSKNEKALGRKINSWESSRSGHSFLSNL 167
          200 TFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMVYVTKTSIKIPSSHTLMKGG 259
Qу
                 Db
          168 HLRNGELVIHEKGFYYIYSQTYFRFQEEIKENTKNDKQMVQYIYKYT-SYPDPILLMKSA 226
          260 STKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLDPDODATYFGAFKV 313
Qγ
                  227 RNSCWSKDAEYGLYSIYQGGIFELKENDRIFVSVTNEHLIDMDHEASFFGAFLV 280
RESULT 5
TN10 MOUSE
     TN10 MOUSE STANDARD; PRT; 291 AA.
     P50592;
AC
     01-OCT-1996 (Rel. 34, Created)
     01-OCT-1996 (Rel. 34, Last sequence update)
DT
     28-FEB-2003 (Rel. 41, Last annotation update)
DT
     Tumor necrosis factor ligand superfamily member 10 (TNF-related
DE
DE
     apoptosis inducing ligand) (TRAIL protein).
     TNFSF10 OR TRAIL.
GN
     Mus musculus (Mouse).
OS
     Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
OC
     Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
```

```
OX
    NCBI TaxID=10090;
RN
    [1]
RP
    SEQUENCE FROM N.A.
RX
    MEDLINE=96111955; PubMed=8777713;
    Wiley S.R., Schooley K., Smolak P.J., Din W.S., Huang C.-P.,
RA
    Nicholl J.K., Sutherland G.R., Davis-Smith T., Rauch C., Smith C.A.,
RA
RA
    Goodwin R.G.;
RT
    "Identification and characterization of a new member of the TNF
RT
    family that induces apoptosis.";
RL
    Immunity 3:673-682(1995).
CC
    -!- FUNCTION: Cytokine that binds to TNFRSF10A/TRAILR1,
CC
        TNFRSF10B/TRAILR2, TNFRSF10C/TRAILR3, TNFRSF10D/TRAILR4 and
CC
        possibly also to TNFRSF11B/OPG. Induces apoptosis. Its activity
CC
        may be modulated by binding to the decoy receptors
CC
        TNFRSF10C/TRAILR3, TNFRSF10D/TRAILR4 and TNFRSF11B/OPG that cannot
CC
        induce apoptosis.
    -!- SUBUNIT: Homotrimer (By similarity).
CC
CC
    -!- SUBCELLULAR LOCATION: Type II membrane protein (Potential).
CC
    -!- TISSUE SPECIFICITY: WIDESPREAD.
CC
    -!- SIMILARITY: Belongs to the tumor necrosis factor family.
CC
    -----
CC
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    or send an email to license@isb-sib.ch).
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    ______
DR
    EMBL; U37522; AAC52345.1; -.
DR
    HSSP; P50591; 1D0G.
DR
    MGD; MGI:107414; Tnfsf10.
DR
    InterPro; IPR006052; TNF family.
DR
    InterPro; IPR008983; TNF like.
    InterPro; IPR003636; TNF subf.
    Pfam; PF00229; TNF; 1.
    ProDom; PD002012; TNF subf; 1.
DR
    SMART; SM00207; TNF; 1.
DR
DR
    PROSITE; PS00251; TNF 1; 1.
DR
    PROSITE; PS50049; TNF 2; 1.
    Cytokine; Transmembrane; Signal-anchor; Apoptosis.
FT
    DOMAIN
                1
                   17
                            CYTOPLASMIC (POTENTIAL).
    TRANSMEM
                      38
FT
                18
                              SIGNAL-ANCHOR (TYPE-II MEMBRANE PROTEIN)
FT
                               (POTENTIAL).
    DOMAIN 39 291 EXTRACELLULAR (POTENTIAL).
CARBOHYD 52 52 N-LINKED (GLCNAC...) (POTENTIAL).
FT
FT
    SEQUENCE 291 AA; 33477 MW; 3FEACAB9F0D7D802 CRC64;
                       14.7%; Score 248; DB 1; Length 291;
 Best Local Similarity 25.4%; Pred. No. 4.9e-14;
         79; Conservative 52; Mismatches 100; Indels 80; Gaps
          46 RSMFVALLGLG-LGQVVCSVALFFYFRAQMD--PNRISEDGTHCIYRILRLHENADFQDT 102
Qу
            Db
         17 RMMVICIVLLQVLLQAVSVAVTYMYFTNEMKQLQDNYSKIGLACFSK----TDEDFWDS 71
        103 TLESQDTKLIPDSCRRIK-----QAFQ-----GAVQKEL 131
QУ
```

```
| ::: | ::|
                                         : ||
Db
          72 T----DGEILNRPCLQVKRQLYQLIEEVTLRTFQDTISTVPEKQLSTPPLPRGGRPOKVA 127
QУ
         132 QHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSHKVSLSSWYHDR 191
              ::| | |
         128 AHITGITR-RSNSALI----PISKDGKTLGQ------KIESWESSR 162
Db
Qу
         192 -GWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYL-----QLMVYV 242
              | : :::: | ||:|:: |:| ||:|: || || || ||::::
Db
         163 KGHSFLNHVLFRNGELVIEQEGLYYIYSQTYFRFQEAED--ASKMVSKDKVRTKQLVQYI 220
         243 TKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLDPD 302
QУ
              Db
         221 YKYT-SYPDPIVLMKSARNSCWSRDAEYGLYSIYQGGLFELKKNDRIFVSVTNEHLMDLD 279
         303 QDATYFGAFKV 313
Qy
             |:|::||| :
Db
         280 QEASFFGAFLI 290
RESULT 6
TNF6 PIG
    TNF6 PIG STANDARD;
ID
                             PRT; 282 AA.
AC
    Q9BEA8; Q95M04; Q95N10;
DT
    28-FEB-2003 (Rel. 41, Created)
DT
    28-FEB-2003 (Rel. 41, Last sequence update)
DT
    10-OCT-2003 (Rel. 42, Last annotation update)
DE
    Tumor necrosis factor ligand superfamily member 6 (FAS antigen
DΕ
    ligand).
    TNFSF6 OR FASL.
GN
OS
    Sus scrofa (Pig).
OC
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Mammalia; Eutheria; Cetartiodactyla; Suina; Suidae; Sus.
OX
    NCBI TaxID=9823;
RN
    [1]
RP
    SEQUENCE FROM N.A.
RX
    MEDLINE=21322533; PubMed=11429161;
RA
    Muneta Y., Shimoji Y., Inumaru S., Mori Y.;
RT
    "Molecular cloning, characterization, and expression of porcine Fas
RT
    ligand (CD95 ligand).";
    J. Interferon Cytokine Res. 21:305-312(2001).
RL
RN
RP
    SEQUENCE FROM N.A.
RC
    STRAIN=Guanxi bama miniature pig;
RA
    Zhu N., Young Y.;
    "Molecular cloning and characterization of porcine Fas ligand cDNA.";
RT
RL
    Submitted (APR-2001) to the EMBL/GenBank/DDBJ databases.
RN
    [3]
RP
    SEQUENCE FROM N.A.
RC
    TISSUE=Lymphoid;
RA
    Tsuyuki S., Kono M., Bloom E.T.;
RT
    "Cloning and potential utility of porcine Fas ligand: overexpression
RT
    in porcine cells protects them from attack by human cytolytic cells.";
RL
    Submitted (JUL-2001) to the EMBL/GenBank/DDBJ databases.
RN
    [4]
RP
    SEQUENCE FROM N.A.
RC
    STRAIN=Landrace x Large Yorkshire white; TISSUE=Thymocytes;
```

```
RX
    MEDLINE=21653191; PubMed=11792426;
    Motegi-Ishiyama Y., Nakajima Y., Hoka S., Takagaki Y.;
RA
RТ
    "Porcine Fas-ligand gene: genomic sequence analysis and comparison
RT
    with human gene.";
RL
    Mol. Immunol. 38:581-586(2002).
CC
    -!- FUNCTION: Cytokine that binds to TNFRSF6/FAS, a receptor that
CC
        transduces the apoptotic signal into cells. May be involved in
CC
        cytotoxic T cell mediated apoptosis and in T cell development.
CC
        TNFRSF6/FAS-mediated apoptosis may have a role in the induction of
CC
        peripheral tolerance, in the antigen-stimulated suicide of mature
CC
        T cells, or both. Binding to the decoy receptor TNFRSF6B/DcR3
CC
        modulates its effects (By similarity).
CC
    -!- SUBUNIT: Homotrimer (Probable).
CC
    -!- SUBCELLULAR LOCATION: Type II membrane protein and secreted (By
CC
        similarity).
CC
    -!- INDUCTION: By IL-18.
CC
    -!- PTM: The soluble form derives from the membrane form by
CC
        proteolytic processing (By similarity).
    -!- SIMILARITY: Belongs to the tumor necrosis factor family.
CC
CC
    ______
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    entities requires a license agreement (See http://www.isb-sib.ch/announce/
    or send an email to license@isb-sib.ch).
CC
CC
    EMBL; AB027297; BAB40919.1; -.
DR
    EMBL; AY033634; AAK56449.1; -.
    EMBL; AF397407; AAK84408.1; -.
DR
DR
    EMBL; AB069764; BAB64291.1; -.
DR
    HSSP; P01375; 4TSV.
    InterPro; IPR008064; Fas ligand.
    InterPro; IPR006053; TNF abc.
DR
    InterPro; IPR006052; TNF family.
DR
    InterPro; IPR008983; TNF like.
DR
    InterPro; IPR003636; TNF subf.
DR
    Pfam; PF00229; TNF; 1.
DR
    PRINTS; PR01681; FASLIGAND.
DR
DR
    PRINTS; PR01234; TNECROSISFCT.
    ProDom; PD002012; TNF subf; 1.
DR
    SMART; SM00207; TNF; 1.
DR
DR
    PROSITE; PS00251; TNF 1; 1.
    PROSITE; PS50049; TNF 2; 1.
DR
KW
    Cytokine; Apoptosis; Transmembrane; Glycoprotein; Signal-anchor.
FT
    CHAIN
                               TUMOR NECROSIS FACTOR LIGAND SUPERFAMILY
                 1
                    282
FT
                               MEMBER 6, MEMBRANE FORM.
FT
    CHAIN
              131
                    282
                               TUMOR NECROSIS FACTOR LIGAND SUPERFAMILY
FT
                               MEMBER 6, SOLUBLE FORM (BY SIMILARITY).
                1
FT
                     82
    DOMAIN
                               CYTOPLASMIC (POTENTIAL).
    TRANSMEM
FT
                83
                      103
                               SIGNAL-ANCHOR (TYPE-II MEMBRANE PROTEIN)
FT
                               (POTENTIAL).
            104 282
FT
    DOMAIN
                              EXTRACELLULAR (POTENTIAL).
    DOMAIN
               4
                     70
FT
                              PRO-RICH.
FT
    DOMAIN
               45
                      56
                              POLY-PRO.
FT
              130
                            CLEAVAGE (BY SIMILARITY).
    SITE
                      131
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DISULFID 203 234 POTENTIAL.

CARBOHYD 185 185 N-LINKED (GLCNAC. . .) (POTENTIAL).

CARBOHYD 251 251 N-LINKED (GLCNAC. . .) (POTENTIAL).

CARBOHYD 261 261 N-LINKED (GLCNAC. . .) (POTENTIAL).

F -> L (IN REF. 4).
FT
FT
FT
FT
     CONFLICT 5 5 F \rightarrow L (IN REF. 4). CONFLICT 57 57 T \rightarrow P (IN REF. 2).
FT
FT
     SEQUENCE 282 AA; 31756 MW; 6743DAA1145671FB CRC64;
SO
  Query Match 11.9%; Score 200; DB 1; Length 282; Best Local Similarity 23.0%; Pred. No. 6.5e-10;
  Matches 76; Conservative 42; Mismatches 90; Indels 122; Gaps 14;
Qу
          22 PGAPHEGPLHAPPPPAPHQPPAA---SRSM-----FVA 51
             11 1 1 111 1 11 :
Db
          37 PGRP--GORRPPPPPPPPPPPTLLPSRPLPPLPPPSLKKKRDHNAGLCLLVMFFMVLVA 94
          52 LLGLGLGQVVCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKL 111
Qу
             1:|||| :| : | : | : |
          95 LVGLGLG-----MFOLFHLOKE------ 124
Db
Qy
         112 IPDSCRRIKQAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAOPFAHLT-- 169
                 : |: :| :: :||
         125 -----ESSLEKQIGHPNLPSEKK-----ELRKVAHLTGK 153
Db
         170 INATDIPSGSHKVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSG 229
Qу
              Db
         154 PNSRSIP-----LEWEDTYGIALVSGVKYMKGSLVINDTGLYFVYSKVYFRGQYCN- 204
         230 DLATEYLQLMVYVTKTSIKIPSSHTLMKGGSTKY-----WSGNSEFHFYSINVGGFFKL 283
Qу
              Db
         205 ----NQPLSHKVY-TRNS-RYPQDLVLMEGKMMNYCTTGQMWARSS------YLGAVFNL 252
         284 RSGEEISIEVSNPSLLDPDQDATYFGAFKV 313
Qу
              253 TSADHLYVNVSELSLVNFEESKTFFGLYKL 282
Db
RESULT 7
TNF6 HUMAN
    TNF6 HUMAN STANDARD; PRT; 281 AA.
ID
    P48023; O9BZP9;
AC
    01-FEB-1996 (Rel. 33, Created)
    01-FEB-1996 (Rel. 33, Last sequence update)
DT
    15-MAR-2004 (Rel. 43, Last annotation update)
DT
    Tumor necrosis factor ligand superfamily member 6 (FAS antigen ligand)
DΕ
DE
     (Apoptosis antigen ligand) (APTL) (CD178 antigen).
GN
    TNFSF6 OR FASL OR APT1LG1.
OS
    Homo sapiens (Human).
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX
    NCBI TaxID=9606;
RN
    [1]
    SEQUENCE FROM N.A. (ISOFORM 1).
RP
    MEDLINE=95105731; PubMed=7528780;
RX
RA
    "Fas ligand mediates activation-induced cell death in human T
RТ
    lymphocytes.";
RT
```

```
RL
     J. Exp. Med. 181:71-77(1995).
RN
R₽
     SEQUENCE FROM N.A. (ISOFORM 1).
RX
     MEDLINE=95127560; PubMed=7826947;
RA
     Takahashi T., Tanaka M., Inazawa J., Abe T., Suda T., Nagata S.;
     "Human Fas ligand: gene structure, chromosomal location and species
RT
RT
     specificity.";
     Int. Immunol. 6:1567-1574(1994).
RL
RN
RΡ
     SEQUENCE FROM N.A. (ISOFORM 1).
RA
     Schaetzlein C.E., Poehlmann R., Philippsen P., Eibel H.;
RL
     Submitted (JUN-1995) to the EMBL/GenBank/DDBJ databases.
RN
RP
     SEQUENCE FROM N.A. (ISOFORM 1).
     MEDLINE=95071350; PubMed=7980502;
RX
RA
     Mita E., Hayashi N., Iio S., Takehara T., Hijioka T., Kasahara A.,
     Fusamoto H., Kamada T.;
RA
RT
     "Role of Fas ligand in apoptosis induced by hepatitis C virus
RΤ
     infection.";
RL
     Biochem. Biophys. Res. Commun. 204:468-474(1994).
RN
RΡ
     SEQUENCE FROM N.A. (ISOFORM 2).
RC
     TISSUE=Leukocyte;
RA
     Zeytun A., Nagarkatti M., Nagarkatti P.S.;
RT
     "Isolation and characterization of a new naturally occuring variant of
RT
     human Fas ligand that is expressed only in membrane bound form.";
RL
     Submitted (JUL-2000) to the EMBL/GenBank/DDBJ databases.
RN
RP
     SEQUENCE FROM N.A.
RA
     Wilkinson J.;
RL
     Submitted (MAY-1997) to the EMBL/GenBank/DDBJ databases.
RN
RP
     SEQUENCE FROM N.A. (ISOFORM 1).
RC
     TISSUE=Blood;
RX
     MEDLINE=22388257; PubMed=12477932;
RA
     Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
RA
     Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
RA
     Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
RA
     Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
RA
     Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
RA
     Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,
RA
     Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
RA
     Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
RA
     Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
RA
     Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
     Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
RA
     Fahey J., Helton E., Ketteman M., Madan A., Rodrigues S., Sanchez A.,
RA
RA
     Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
RA
     Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,
RA
     Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,
RA
     Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,
RA
     Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;
     "Generation and initial analysis of more than 15,000 full-length
RΤ
RT
     human and mouse cDNA sequences.";
RL
     Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
RN
     SEQUENCE OF 1-10 FROM N.A.
RP
```

```
RC
     TISSUE=Blood;
RA
     Matsumura M., Nakanishi Y., Ohba Y.;
RL
     Submitted (APR-1998) to the EMBL/GenBank/DDBJ databases.
RN
RΡ
     CHARACTERIZATION, AND MUTAGENESIS OF PRO-206; TYR-218 AND PHE-275.
RX
     MEDLINE=97373583; PubMed=9228058;
RA
     Schneider P., Bodmer J.-L., Holler N., Mattmann C., Scuderi P.,
RA
     Terskikh A., Peitsch M.C., Tschopp J.;
RT
     "Characterization of Fas (Apo-1, CD95)-Fas ligand interaction.";
RL
     J. Biol. Chem. 272:18827-18833(1997).
RN
     [10]
RP
     PROCESSING.
     MEDLINE=98087475; PubMed=9427603;
RX
RA
     Tanaka M., Itai T., Adachi M., Nagata S.;
RT
     "Downregulation of Fas ligand by shedding.";
RL
     Nat. Med. 4:31-36(1998).
CC
     -!- FUNCTION: Cytokine that binds to TNFRSF6/FAS, a receptor that
CC
         transduces the apoptotic signal into cells. May be involved in
CC
         cytotoxic T cell mediated apoptosis and in T cell development.
CC
         TNFRSF6/FAS-mediated apoptosis may have a role in the induction of
CC
         peripheral tolerance, in the antigen-stimulated suicide of mature
CC
         T cells, or both. Binding to the decoy receptor TNFRSF6B/DcR3
CC
        modulates its effects.
CC
     -!- SUBUNIT: Homotrimer (Probable).
     -!- SUBCELLULAR LOCATION: Type II membrane protein. May be released
CC
         into the extracellular fluid, probably by cleavage form the cell
CC
CC
         surface.
CC
     -!- ALTERNATIVE PRODUCTS:
        Event=Alternative splicing; Named isoforms=2;
CC
CC
CC
          IsoId=P48023-1; Sequence=Displayed;
CC
        Name=2;
CC
          IsoId=P48023-2; Sequence=VSP 006443, VSP 006444;
CC
     -!- PTM: N-glycosylated.
CC
     -!- PTM: The soluble form derives from the membrane form by
CC
        proteolytic processing.
CC
    -!- DISEASE: Defects in TNFSF6 are a cause of autoimmune
CC
        lymphoproliferative syndrome (ALPS) [MIM:601859]; also known as
CC
        Canale-Smith syndrome (CSS). ALPS is a childhood syndrome
        involving hemolytic anemia and thrombocytopenia with massive
CC
CC
        lymphadenopathy and splenomegaly.
CC
     -!- SIMILARITY: Belongs to the tumor necrosis factor family.
CC
    -!- DATABASE: NAME=PROW; NOTE=PROW 2:59-69(2001);
CC
        WWW="http://www.ncbi.nlm.nih.gov/prow/guide/333879674 g.htm".
     CC
CC
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    or send an email to license@isb-sib.ch).
CC
DR
    EMBL; X89102; CAA61474.1; -.
    EMBL; U08137; AAC50071.1; -.
DR
DR
    EMBL; U11821; AAC50124.1; -.
DR
    EMBL; D38122; BAA07320.1; -.
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DR
     EMBL; AF288573; AAG60017.1; -.
DR
     EMBL; Z96050; CAB09424.1; -.
DR
     EMBL; BC017502; AAH17502.1; -.
DR
     EMBL; AB013303; BAA32542.1; -.
     PIR; I38707; I38707.
DR
     HSSP; P01375; 1TNF.
DR
DR
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     MIM; 134638; -.
DR
DR
     MIM; 601859; -.
DR
     GO; GO:0005887; C:integral to plasma membrane; TAS.
DR
     GO; GO:0005102; F:receptor binding; TAS.
     GO; GO:0007267; P:cell-cell signaling; TAS.
DR
DR
     GO; GO:0006917; P:induction of apoptosis; TAS.
DR
     GO; GO:0007165; P:signal transduction; TAS.
DR
     InterPro; IPR008064; Fas ligand.
DR
     InterPro; IPR006053; TNF abc.
DR
     InterPro; IPR006052; TNF_family.
DR
     InterPro; IPR008983; TNF like.
     InterPro; IPR003636; TNF_subf.
DR
DR
     Pfam; PF00229; TNF; 1.
DR
     PRINTS; PR01681; FASLIGAND.
     PRINTS; PR01234; TNECROSISFCT.
DR
     ProDom; PD002012; TNF subf; 1.
     SMART; SM00207; TNF; 1.
DR
     PROSITE; PS00251; TNF_1; 1.
DR
     PROSITE; PS50049; TNF 2; 1.
DR
KW
     Cytokine; Apoptosis; Transmembrane; Glycoprotein; Signal-anchor;
KW
     Alternative splicing; Antigen.
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FT
     CHAIN
                   1
                        281
FT
                                   MEMBER 6, MEMBRANE FORM.
FT
     CHAIN
                 130
                        281
                                   TUMOR NECROSIS FACTOR LIGAND SUPERFAMILY
FT
                                   MEMBER 6, SOLUBLE FORM.
FT
     DOMAIN
                  1
                         80
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FT
     TRANSMEM
                  81
                        102
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FT
                                   (POTENTIAL).
FT
                 103
     DOMAIN
                        281
                                  EXTRACELLULAR (POTENTIAL).
FT
     DOMAIN
                  4
                         70
                                  PRO-RICH.
FT
     DOMAIN
                  45
                         65
                                  POLY-PRO.
FT
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                 129
                        130
                                  CLEAVAGE.
FT
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FT
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                        184
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FT
                 250
     CARBOHYD
                      250
                                  N-LINKED (GLCNAC. . .) (POTENTIAL).
FT
     CARBOHYD
                 260
                        260
                                  N-LINKED (GLCNAC. . .) (POTENTIAL).
FT
    VARSPLIC
                 117
                        127
                                  STSQMHTASSL -> ATPVHPLKKRS (in isoform
FT
FT
                                  /FTId=VSP 006443.
FT
    VARSPLIC
                 128
                        281
                                  Missing (in isoform 2).
FT
                                  /FTId=VSP 006444.
FT
    MUTAGEN
                 206
                        206
                                  P->D, F, R: LOWERS BINDING TO TNFRSF6 AND
FT
                                  REDUCES CYTOTOXITY MORE THAN 100-FOLD.
FT
    MUTAGEN
                 218
                        218
                                  Y->F,R: LOWERS BINDING TO TNFRSF6 AND
FT
                                  ABOLISHES CYTOTOXITY.
FT
    MUTAGEN
                 275
                        275
                                  F->L: ABOLISHES BINDING TO TNRFSF6 AND
FT
                                  CYTOTOXICITY.
SQ
     SEQUENCE
                281 AA; 31485 MW; A8A6EB358246E9BB CRC64;
  Query Match
                         11.2%; Score 189; DB 1; Length 281;
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Best Local Similarity 21.7%; Pred. No. 5.8e-09;
  Matches 69; Conservative 43; Mismatches 98; Indels 108; Gaps 11;
         22 PGAPHEGPLHAPPPPAP----HQPPAASRS------MFVALLGLGLGQVVCS 63
QУ
            Db
         46 PPPPPPPPPPPPPPPPPPPPLPPLPPLKKRGNHSTGLCLLVMFFMVLVALVGLGLG---- 100
         64 VALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIKQAF 123
QУ
             : 1 1 1
                       | |: :::| :
         101 --MFQLFHLQ------ 124
Db
        124 QGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLT--INATDIPSGSHK 181
QУ
             :::|:: |
                        | | : | | | | : : |
        125 -SSLEKQIGH----- 159
Db
Qу
        182 VSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMVY 241
               Db
        160 ---LEWEDTYGIVLLSGVKYKKGGLVINETGLYFVYSKVYFRGOSCNN-----LPLSHK 210
        242 VTKTSIKIPSSHTLMKGGSTKY-----WSGNSEFHFYSINVGGFFKLRSGEEISIEVSN 295
QУ
            1 : | | : | : | : : | : : | |
        211 VYMRNSKYPQDLVMMEGKMMSYCTTGQMWARSS-----YLGAVFNLTSADHLYVNVSE 263
Db
        296 PSLLDPDODATYFGAFKV 313
QУ
            Db
        264 LSLVNFEESQTFFGLYKL 281
RESULT 8
TNF6 MACMU
    TNF6 MACMU
               STANDARD; PRT; 280 AA.
    Q9MYL6; Q9BDM5;
    28-FEB-2003 (Rel. 41, Created)
DT
DT
    28-FEB-2003 (Rel. 41, Last sequence update)
DT
    28-FEB-2003 (Rel. 41, Last annotation update)
    Tumor necrosis factor ligand superfamily member 6 (FAS antigen ligand)
DE
    (CD95L protein).
    TNFSF6 OR FASL OR CD95L.
GN
OS
    Macaca mulatta (Rhesus macaque),
    Macaca fascicularis (Crab eating macaque) (Cynomolgus monkey), and
OS
OS
    Macaca nemestrina (Pig-tailed macaque).
OC
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
    Mammalia; Eutheria; Primates; Catarrhini; Cercopithecidae;
OC
OC
    Cercopithecinae; Macaca.
OX
    NCBI TaxID=9544, 9541, 9545;
RN
    [1]
RP
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RC
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RX
    MEDLINE=21383618; PubMed=11491535;
RA
    Villinger F., Bostik P., Mayne A.E., King C.L., Genain C.P.,
RA
    Weiss W.R., Ansari A.A.;
RT
    "Cloning, sequencing, and homology analysis of nonhuman primate
RT
    Fas/Fas-ligand and co-stimulatory molecules.";
RL
    Immunogenetics 53:315-328(2001).
RN
    [2]
RP
    SEQUENCE FROM N.A.
RC
    SPECIES=M.mulatta, M.fascicularis, and M.nemestrina;
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RA
     Kirii Y., Inoue T., Yoshino K.;
RL
     Submitted (NOV-1999) to the EMBL/GenBank/DDBJ databases.
CC
     -!- FUNCTION: Cytokine that binds to TNFRSF6/FAS, a receptor that
CC
         transduces the apoptotic signal into cells. May be involved in
CC
         cytotoxic T cell mediated apoptosis and in T cell development.
CC
        TNFRSF6/FAS-mediated apoptosis may have a role in the induction of
CC
         peripheral tolerance, in the antigen-stimulated suicide of mature
CC
        T cells, or both. Binding to the decoy receptor {\tt TNFRSF6B/DcR3}
CC
        modulates its effects (By similarity).
CC
     -!- SUBUNIT: Homotrimer (Potential).
     -!- SUBCELLULAR LOCATION: Type II membrane protein and secreted (By
CC
CC
        similarity).
CC
     -!- PTM: The soluble form derives from the membrane form by
CC
        proteolytic processing (By similarity).
CC
     -!- SIMILARITY: Belongs to the tumor necrosis factor family.
CC
     _____
CC
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     between the Swiss Institute of Bioinformatics and the EMBL outstation -
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     the European Bioinformatics Institute. There are no restrictions on its
     use by non-profit institutions as long as its content is in no way
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     modified and this statement is not removed. Usage by and for commercial
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     entities requires a license agreement (See http://www.isb-sib.ch/announce/
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     or send an email to license@isb-sib.ch).
CC
CC
     ______
DR
     EMBL; AF344856; AAK37539.1; -.
DR
     EMBL; AB035138; BAA90294.1; -.
    EMBL; AB035139; BAA90295.1; -.
DR
DR
    EMBL; AB035140; BAA90296.1; -.
    HSSP; P01375; 4TSV.
DR
    InterPro; IPR008064; Fas ligand.
    InterPro; IPR006053; TNF abc.
DR
    InterPro; IPR006052; TNF_family.
DR
DR
    InterPro; IPR008983; TNF like.
DR
    InterPro; IPR003636; TNF subf.
DR
    Pfam; PF00229; TNF; 1.
    PRINTS; PR01681; FASLIGAND.
    PRINTS; PR01234; TNECROSISFCT.
DR
    ProDom; PD002012; TNF subf; 1.
DR
    SMART; SM00207; TNF; 1.
DR
    PROSITE; PS00251; TNF 1; 1.
DR
    PROSITE; PS50049; TNF 2; 1.
    Cytokine; Apoptosis; Transmembrane; Glycoprotein; Signal-anchor.
KW
FT
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                 1
                      280
                                TUMOR NECROSIS FACTOR LIGAND SUPERFAMILY
FT
                                MEMBER 6, MEMBRANE FORM.
FT
    CHAIN
                129
                      280
                                TUMOR NECROSIS FACTOR LIGAND SUPERFAMILY
FT
                                MEMBER 6, SOLUBLE FORM (BY SIMILARITY).
FT
    DOMAIN
                 1
                       80
                                CYTOPLASMIC (POTENTIAL).
FT
    TRANSMEM
                81
                      101
                                SIGNAL-ANCHOR (TYPE-II MEMBRANE PROTEIN)
FT
                                (POTENTIAL).
FT
    DOMAIN
                102
                     280
                                EXTRACELLULAR (POTENTIAL).
FT
    DOMAIN
                4
                      69
                                PRO-RICH.
FT
    DOMAIN
                45
                      64
                                POLY-PRO.
FT
                128
                                CLEAVAGE (BY SIMILARITY).
    SITE
                      129
FT
    DISULFID
                201
                     232
                               POTENTIAL.
FT
              183
    CARBOHYD
                    183
                               N-LINKED (GLCNAC. . .) (POTENTIAL).
FT
               249
    CARBOHYD
                    249
                               N-LINKED (GLCNAC. . .) (POTENTIAL).
FT
    CARBOHYD
               259
                     259
                              N-LINKED (GLCNAC. . .) (POTENTIAL).
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FT
                    60 S \rightarrow P (IN REF. 1).
    CONFLICT
              60
    SEQUENCE 280 AA; 31367 MW; F0B284D61A132EB4 CRC64;
SQ
  Query Match
                      11.0%; Score 186; DB 1; Length 280;
  Best Local Similarity 22.1%; Pred. No. 1e-08;
         69; Conservative 44; Mismatches 103; Indels 96; Gaps
                                                                 11:
         22 PGAPHEGPLHAPPPPAP----HQPPAASRS------MFVALLGLGLGQVVCS 63
QУ
            Db
         45 PPPPPPPPPPPPPPPPPPPPPPPPLPLPPLKKRGNHSTGLCLLVMFFMVLVALVGLGLG---- 99
         64 VALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIKQAF 123
QУ
             : | | |
                      | |: :::| :
        100 --MFQLFHLQ------ 123
Db
        124 QGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLT--INATDIPSGSHK 181
QУ
                        11: 1111
             :::|::|
                                                    |: :|
        124 -SSLEKQIGH----- 158
Db
        182 VSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMVY 241
Qу
             159 ---LEWEDTYGIVLLSGVKYKKGGLVINETGLYFVYSKVYFR-----GQSCTN-LPLSHK 209
Db
        242 VTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLDP 301
Qу
            Db
        210 VYMRNSKYPQDLVMMEGKMMSYCT-TGQMWAHSSYLGAVFNLTSADHLYVNVSELSLVNF 268
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Qу
           :: |:|| :|:
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Db
RESULT 9
TNF6 MOUSE
ID
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               STANDARD; PRT; 279 AA.
    P41047; Q61217; Q9R1F2;
AC
DT
    01-FEB-1995 (Rel. 31, Created)
    01-FEB-1995 (Rel. 31, Last sequence update)
    15-MAR-2004 (Rel. 43, Last annotation update)
DT
    Tumor necrosis factor ligand superfamily member 6 (FAS antigen
DE
DE
    ligand).
    TNFSF6 OR FASL OR APTILG1 OR GLD.
GN
OS
    Mus musculus (Mouse).
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
OC
    Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX
    NCBI TaxID=10090;
RN
    [1]
RP
    SEQUENCE FROM N.A. (ISOFORM FASL).
    MEDLINE=94185175; PubMed=7511063;
RX
RA
    Takahashi T., Tanaka M., Brannan C.I., Jenkins N.A., Copeland N.G.,
RA
    Suda T., Nagata S.;
RT
    "Generalized lymphoproliferative disease in mice, caused by a point
RТ
    mutation in the Fas ligand.";
RL
    Cell 76:969-976(1994).
RN
RP
    SEQUENCE FROM N.A. (ISOFORM FASL), AND 3D-STRUCTURE MODELING.
RC
    STRAIN=C57BL/6;
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RX
     MEDLINE=95388076; PubMed=7544870;
RA
     Peitsch M.J., Tschopp J.J.;
RT
      "Comparative molecular modelling of the Fas-ligand and other members
RT
     of the TNF family.";
RL
     Mol. Immunol. 32:761-772(1995).
RN
RP
     SEQUENCE FROM N.A. (ISOFORM FASL).
RX
     MEDLINE=95196085; PubMed=7889405;
     Lynch D.H., Watson M.L., Alderson M.R., Baum P.R., Miller R.E.,
RA
     Tough T., Gibson M., Davis-Smith T., Smith C.A., Hunter K.;
RA
     "The mouse Fas-ligand gene is mutated in gld mice and is part of a
RT
     TNF family gene cluster.";
RT
RL
     Immunity 1:131-136(1994).
RN
     [4]
RP
     SEQUENCE FROM N.A. (ISOFORM FASL).
RC
     STRAIN=BALB/c;
RA
     Fenner M.H., Shioda T., Isselbacher K.J.;
RТ
     "Mus musculus Balb/c Fas ligand differs from 129/SV Fas ligand in
RT
     two amino acids.";
RL
     Submitted (MAY-1996) to the EMBL/GenBank/DDBJ databases.
RN
RP
     SEQUENCE FROM N.A. (ISOFORM FASLS).
RC
     STRAIN=C3H; TISSUE=Spleen;
     MEDLINE=20021694; PubMed=10552956;
RA
     Ayroldi E., D'Adamio F., Zollo O., Agostini M., Moraca R.,
RA
     Cannarile L., Migliorati G., Delfino D.V., Riccardi C.;
RT
     "Cloning and expression of a short Fas ligand: A new alternatively
RT
     spliced product of the mouse Fas ligand gene.";
     Blood 94:3456-3467(1999).
RL
RN
RP
     CHARACTERIZATION OF VARIANT GLD.
RX
     MEDLINE=96091792; PubMed=7495745;
RA
     Hahne M., Peitsch M.C., Irmler M., Schroeter M., Lowin B.,
     Rousseau M., Bron C., Renno T., French L., Tschopp J.;
RA
     "Characterization of the non-functional Fas ligand of gld mice.";
RT
RL
     Int. Immunol. 7:1381-1386(1995).
RN
RP
     VARIANTS ALA-184 AND GLY-218.
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     STRAIN=C57BL/6, C3H, MRL, SJL, NOD, NZB, NZW, BALB/c, DBA/1, and
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     MEDLINE=97268671; PubMed=9108079;
     Kayagaki N., Yamaguchi N., Nagao F., Matsuo S., Maeda H., Okumura K.,
RA
RA
     Yagita H.;
RT
     "Polymorphism of murine Fas ligand that affects the biological
RT
     activity.";
     Proc. Natl. Acad. Sci. U.S.A. 94:3914-3919(1997).
RL
CC
     -!- FUNCTION: Cytokine that binds to TNFRSF6/FAS, a receptor that
CC
         transduces the apoptotic signal into cells. May be involved in
CC
         cytotoxic T cell mediated apoptosis and in T cell development.
CC
         TNFRSF6/FAS-mediated apoptosis may have a role in the induction of
CC
         peripheral tolerance, in the antigen-stimulated suicide of mature
         T cells, or both. Binding to the decoy receptor TNFRSF6B/DcR3
CC
CC
         modulates its effects (By similarity).
CC
     -!- SUBUNIT: Homotrimer (Probable).
CC
     -!- SUBCELLULAR LOCATION: Type II membrane protein (isoform FASL);
CC
         Secreted (isoforms FASL and FASLS).
CC
     -!- ALTERNATIVE PRODUCTS:
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Event=Alternative splicing; Named isoforms=2;
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         Name=FasL;
CC
           IsoId=P41047-1; Sequence=Displayed;
CC
         Name=FasLS;
CC
           IsoId=P41047-2; Sequence=VSP 006445;
CC
     -!- PTM: The soluble form derives from the membrane form by
CC
        proteolytic processing (By similarity).
CC
     -!- DISEASE: A deficiency in this protein is the cause of generalized
         lymphoproliferation disease phenotype (gld). Gld mice present
CC
CC
         lymphadenopathy and autoantibody production. The phenotype is
CC
         recessively inherited.
CC
     -!- SIMILARITY: Belongs to the tumor necrosis factor family.
     _____
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     between the Swiss Institute of Bioinformatics and the EMBL outstation -
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     or send an email to license@isb-sib.ch).
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     ______
DR
     EMBL; U06948; AAA17800.1; -.
DR
     EMBL; U10984; AAA19778.1; -.
DR
     EMBL; S76752; AAB33780.1; -.
     EMBL; U58995; AAB02915.1; -.
DR
     EMBL; AF119335; AAD52106.1; -.
DR
DR
     PIR; A53062; A53062.
DR
    HSSP; P01375; 4TSV.
DR
    MGD; MGI:99255; Tnfsf6.
DR
    InterPro; IPR008064; Fas ligand.
    InterPro; IPR006053; TNF abc.
DR
    InterPro; IPR006052; TNF family.
DR
    InterPro; IPR008983; TNF like.
DR
DR
    InterPro; IPR003636; TNF subf.
DR
    Pfam; PF00229; TNF; 1.
DR
    PRINTS; PR01681; FASLIGAND.
DR
    PRINTS; PR01234; TNECROSISFCT.
    ProDom; PD002012; TNF subf; 1.
DR
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    PROSITE; PS00251; TNF 1; 1.
DR
    PROSITE; PS50049; TNF_2; 1.
DR
KW
    Cytokine; Apoptosis; Transmembrane; Glycoprotein; Signal-anchor;
KW
    Disease mutation; Polymorphism; Alternative splicing.
FT
    CHAIN
                                TUMOR NECROSIS FACTOR LIGAND SUPERFAMILY
                  1
                      279
FT
                                MEMBER 6, MEMBRANE FORM.
FT
    CHAIN
                128
                      279
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FT
                                MEMBER 6, SOLUBLE FORM (BY SIMILARITY).
                 1
FT
                       78
    DOMAIN
                                CYTOPLASMIC (POTENTIAL).
FT
    TRANSMEM
                79
                      100
                                SIGNAL-ANCHOR (TYPE-II MEMBRANE PROTEIN)
FT
                                (POTENTIAL).
FT
    DOMAIN
                101
                      279
                                EXTRACELLULAR (POTENTIAL).
FT
    DOMAIN
                4
                      69
                                PRO-RICH.
FT
   DOMAIN
                45
                      51
                                POLY-PRO.
FT
    SITE
                127
                      128
                                CLEAVAGE (BY SIMILARITY).
FT
    DISULFID
               200
                      231
                               POTENTIAL.
FT
    CARBOHYD
               117
                     117
                                N-LINKED (GLCNAC. . .) (POTENTIAL).
FT
    CARBOHYD
               182
                     182
                                N-LINKED (GLCNAC. . .) (POTENTIAL).
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CC

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FT
     CARBOHYD
               248
                     248
                             N-LINKED (GLCNAC. . .) (POTENTIAL).
FT
     CARBOHYD
               258
                             N-LINKED (GLCNAC. . .) (POTENTIAL).
                     258
FT
     VARSPLIC
               1
                     210
                             Missing (in isoform FasLS).
FT
                             /FTId=VSP 006445.
FT
    VARIANT
              184
                     184
                             T -> A (\overline{\text{IN}} STRAINS BALB/C AND DBA;
FT
                             ENHANCES CYTOTOXICITY).
FT
    VARIANT
             218
                     218
                             E -> G (IN STRAINS BALB/C AND DBA;
FT
                             ENHANCES CYTOTOXICITY).
    VARIANT 273
FT
                    273
                             F -> L (IN GLD; ABOLISHES BINDING OF FASL
FT
                             TO ITS RECEPTOR).
SO
    SEQUENCE 279 AA; 31442 MW; 37972E2728E0A1CA CRC64;
  Query Match
                     10.9%; Score 184.5; DB 1; Length 279;
  Best Local Similarity 21.7%; Pred. No. 1.4e-08;
  Matches 70; Conservative 45; Mismatches 106; Indels 101; Gaps
Qу
         13 RGSEEMGGGPGAPHEGPLHAPPPPAPHQP-----PAASRSMFVALLGLGL 57
                   38 RGPDQRRPPPPPPPVSPLPPPSQPLPLPPLTPLKKKDHNTNLWLPVVFFMVLVALVGMGL 97
Db
         58 GQVVCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCR 117
Qу
                    :|:: |
         Db
        118 RIKQAFQGAVQKELQHI--VGSQHIRA---EKAMVDGSWLDLAKRSKLEAQPFAHLTINA 172
Qy
                   106 ------QKELAELREFTNQSLKVSSFEKQIANPS----TPSEKKEPRSVAHLTGN- 150
Db
        173 TDIPSGSHKVSLS-SWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDL 231
Qу
                 151 -----PHSRSIPLEWEDTYGTALISGVKYKKGGLVINETGLYFVYSKVYFRGQSCN--- 201
Db
        232 ATEYLQLMVYVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISI 291
QУ
              202 -NQPLNHKVYMRNS--KYPEDLVLMEEKRLNYCT-TGQIWAHSSYLGAVFNLTSADHLYV 257
Db
Qу
        292 EVSNPSLLDPDQDATYFGAFKV 313
            :| ||:: :: |:|| :|:
Db
        258 NISQLSLINFEESKTFFGLYKL 279
RESULT 10
TNF6 CERTO
ΙD
    TNF6 CERTO
               STANDARD; PRT; 280 AA.
AC
    Q9BDN1;
    28-FEB-2003 (Rel. 41, Created)
    28-FEB-2003 (Rel. 41, Last sequence update)
    28-FEB-2003 (Rel. 41, Last annotation update)
DT
    Tumor necrosis factor ligand superfamily member 6 (FAS antigen ligand)
DE
    (CD95L protein).
GN
   TNFSF6 OR FASL OR CD95L.
    Cercocebus torquatus atys (Red-crowned mangabey) (Sooty mangabey).
OS
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Mammalia; Eutheria; Primates; Catarrhini; Cercopithecidae;
OC
    Cercopithecinae; Cercocebus.
OX
    NCBI TaxID=9531;
RN
   [1]
```

```
RΡ
     SEQUENCE FROM N.A.
RC
     TISSUE=Lymphocytes;
RX
     MEDLINE=21383618; PubMed=11491535;
RA
     Villinger F., Bostik P., Mayne A.E., King C.L., Genain C.P.,
RA
     Weiss W.R., Ansari A.A.;
RT
     "Cloning, sequencing, and homology analysis of nonhuman primate
RT
     Fas/Fas-ligand and co-stimulatory molecules.";
RL
     Immunogenetics 53:315-328(2001).
CC
     -!- FUNCTION: Cytokine that binds to TNFRSF6/FAS, a receptor that
CC
         transduces the apoptotic signal into cells. May be involved in
CC
         cytotoxic T cell mediated apoptosis and in T cell development.
CC
        TNFRSF6/FAS-mediated apoptosis may have a role in the induction of
CC
        peripheral tolerance, in the antigen-stimulated suicide of mature
CC
        T cells, or both. Binding to the decoy receptor {\tt TNFRSF6B/DcR3}
CC
        modulates its effects (By similarity).
CC
     -!- SUBUNIT: Homotrimer (Probable).
CC
     -!- SUBCELLULAR LOCATION: Type II membrane protein and secreted (By
CC
        similarity).
CC
     -!- PTM: The soluble form derives from the membrane form by
CC
        proteolytic processing (By similarity).
     -!- SIMILARITY: Belongs to the tumor necrosis factor family.
CC
CC
     CC
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     or send an email to license@isb-sib.ch).
CC
    ______
CC
DR
    EMBL; AF344847; AAK37606.1; -.
DR
    HSSP; P01375; 4TSV.
    InterPro; IPR008064; Fas ligand.
DR
DR
    InterPro; IPR006053; TNF abc.
DR
    InterPro; IPR006052; TNF family.
DR
    InterPro; IPR008983; TNF like.
    InterPro; IPR003636; TNF subf.
    Pfam; PF00229; TNF; 1.
    PRINTS; PR01681; FASLIGAND.
DR
    PRINTS; PR01234; TNECROSISFCT.
DR
DR
    ProDom; PD002012; TNF subf; 1.
DR
    SMART; SM00207; TNF; \overline{1}.
DR
    PROSITE; PS00251; TNF 1; 1.
DR
    PROSITE; PS50049; TNF 2; 1.
    Cytokine; Apoptosis; Transmembrane; Glycoprotein; Signal-anchor.
FT
    CHAIN
                1 280
                                TUMOR NECROSIS FACTOR LIGAND SUPERFAMILY
FT
                                MEMBER 6, MEMBRANE FORM.
FT
    CHAIN
               129
                      280
                                TUMOR NECROSIS FACTOR LIGAND SUPERFAMILY
FT
                               MEMBER 6, SOLUBLE FORM (BY SIMILARITY).
FT
    DOMAIN
                1
                       80
                                CYTOPLASMIC (POTENTIAL).
FT
    TRANSMEM
               81
                      101
                               SIGNAL-ANCHOR (TYPE-II MEMBRANE PROTEIN)
FT
                                (POTENTIAL).
FT
    DOMAIN
               102
                      280
                               EXTRACELLULAR (POTENTIAL).
                     69
FT
    DOMAIN
                4
                               PRO-RICH.
FT
    DOMAIN
                45
                      64
                               POLY-PRO.
FT
    SITE
               128
                      129
                              CLEAVAGE (BY SIMILARITY).
FT
   DISULFID 201
                    232
                              POTENTIAL.
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CARBOHYD 183 183 N-LINKED (GLCNAC. . .) (POTENTIAL).
CARBOHYD 249 249 N-LINKED (GLCNAC. . .) (POTENTIAL).
CARBOHYD 259 259 N-LINKED (GLCNAC. . .) (POTENTIAL).
FT
FT
FT
SQ
    SEQUENCE 280 AA; 31407 MW; 729EA60067B7D398 CRC64;
  Query Match
                      10.8%; Score 182.5; DB 1; Length 280;
  Best Local Similarity 22.4%; Pred. No. 2.1e-08;
  Matches 70; Conservative 44; Mismatches 100; Indels 99; Gaps 12;
          22 PGAPHEGPLHAPPPPAPHQPP-----AASRS-----MFVALLGLGLGQVVC 62
QУ
            Db
          46 PPPPPPPPL--PPPPPPPPLPPLPPLKKRGNHSTGLCLLVMFFMVLVALVGLGLG---- 99
          63 SVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIKQA 122
Qу
             100 ---MFQLFHLQ------ 123
Db
         123 FQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLT--INATDIPSGSH 180
Qу
                            | | : | | | : : |
         124 --SSLEKQIGH----- 158
Db
Qy
        181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
               Db
         159 ----LEWEDTYGIVLLSGVKYKKGGLVINETGLYFVYSKVYFR-----GQSCTN-LPLSH 208
        241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Qу
             209 KVYMRNSKYPQDLVMMEGKMMSYCT-TGQMWAHSSYLGAVFNLTSTDHLYVNVSELSLVN 267
Db
Qу
        301 PDQDATYFGAFKV 313
            :: |:|| :|:
Db
        268 FEESQTFFGLYKL 280
RESULT 11
TNF5 BOVIN
    TNF5 BOVIN
                STANDARD; PRT; 261 AA.
AC
    P51749;
DT
    01-OCT-1996 (Rel. 34, Created)
    01-OCT-1996 (Rel. 34, Last sequence update)
    28-FEB-2003 (Rel. 41, Last annotation update)
DΤ
DE Tumor necrosis factor ligand superfamily member 5 (CD40 ligand) (TNF-
DE related activation protein) (TRAP) (T cell antigen GP39).
GN
    TNFSF5 OR CD40LG OR CD40L.
OS
    Bos taurus (Bovine).
OC
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovoidea;
OC
    Bovidae; Bovinae; Bos.
OX
    NCBI TaxID=9913;
RN
RP
    SEQUENCE FROM N.A.
RC
    TISSUE=Blood;
RX
    MEDLINE=96006582; PubMed=7590981;
RA
    Mertens B.E.L.C., Muriuki M., Gaidulis L.;
RT
    "Cloning of two members of the TNF-superfamily in cattle: CD40 ligand
RT
    and tumor necrosis factor alpha.";
RL
    Immunogenetics 42:430-431(1995).
```

```
CC
     -!- FUNCTION: Cytokine that binds to TNFRSF5. Mediates B-cell
CC
         proliferation in the absence of co-stimulus as well as IqE
CC
         production in the presence of IL-4. Involved in immunoglobulin
CC
         class switching (By similarity).
CC
     -!- SUBUNIT: Homotrimer (By similarity).
CC
     -!- SUBCELLULAR LOCATION: Type II membrane protein. Also exists as an
CC
         extracellular soluble form (By similarity).
CC
     -!- PTM: The soluble form derives from the membrane form by
CC
         proteolytic processing (By similarity).
     -!- SIMILARITY: Belongs to the tumor necrosis factor family.
CC
     ______
CC
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     or send an email to license@isb-sib.ch).
CC
DR
     EMBL; Z48469; CAA88363.1; -.
DR
     PIR; S53090; S53090.
DR
     HSSP; P29965; 1ALY.
     GO; GO:0016021; C:integral to membrane; ISS.
     GO; GO:0005174; F:CD40 receptor binding; ISS.
DR
     GO; GO:0042100; P:B-cell proliferation; ISS.
DR
DR
     GO; GO:0006954; P:inflammatory response; ISS.
     GO; GO:0007159; P:leukocyte cell adhesion; ISS.
DR
DR
     GO; GO:0030168; P:platelet activation; ISS.
DR
    InterPro; IPR003263; TNF 5.
DR
    InterPro; IPR006052; TNF family.
DR
    InterPro; IPR008983; TNF like.
DR
    InterPro; IPR003636; TNF subf.
DR
    Pfam; PF00229; TNF; 1.
DR
    PRINTS; PR01702; CD40LIGAND.
DR
    ProDom; PD008600; TNF 5; 1.
DR
    ProDom; PD002012; TNF subf; 1.
DR
    SMART; SM00207; TNF; \overline{1}.
    PROSITE; PS00251; TNF 1; 1.
    PROSITE; PS50049; TNF 2; 1.
DR
    Cytokine; Transmembrane; Glycoprotein; Signal-anchor.
KW
FT
    CHAIN
                  1
                     261
                                TUMOR NECROSIS FACTOR LIGAND SUPERFAMILY
FT
                                MEMBER 5, MEMBRANE FORM.
FT
    CHAIN
                113
                       261
                                TUMOR NECROSIS FACTOR LIGAND SUPERFAMILY
FT
                                MEMBER 5, SOLUBLE FORM (BY SIMILARITY).
                 1
FT
    DOMAIN
                       22
                                CYTOPLASMIC (POTENTIAL).
ਧਾਜ
    TRANSMEM
                 23
                       46
                                SIGNAL-ANCHOR (TYPE-II MEMBRANE PROTEIN)
FT
                                (POTENTIAL).
FT
    DOMAIN
                47
                    261
                                EXTRACELLULAR (POTENTIAL).
FT
    SITE
               112 113
                                CLEAVAGE (BY SIMILARITY).
FT
    DISULFID 178
                      218
                                POTENTIAL.
FT
    CARBOHYD
               240
                      240
                              N-LINKED (GLCNAC. . .) (POTENTIAL).
    SEQUENCE 261 AA; 29242 MW; 8491FEFB30A787FD CRC64;
 Query Match
                        10.5%; Score 176.5; DB 1; Length 261;
 Best Local Similarity 24.2%; Pred. No. 6.3e-08;
 Matches 70; Conservative 54; Mismatches 122; Indels 43; Gaps 13;
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33 PPPPAPHQPPAASRSMFVALLGLGL-GQVVCSVALFFYFRAQMDPNRISEDGTHCIYRIL 91
 Qу
              Db
            8 PSPRSVATGPPVSMKIFMYLLTVFLITQMIGSALFAVYLHRRLD--KIEDE----R 57
           92 RLHENADFQDT--TLESQDTKLIPDSCRRIKQAFQGAVQKELQHIVGSQHIRAEKAMVDG 149
 Qу
               :: :: :: :
Db
           58 NLHEDFVFMKTIQRCNKGEGSLSLLNCEEIRSRFEDLVKDIMQ---NKEVKKKEKNFE- 112
          150 SWLDLAKRSKLEAQPFAHLTINATDIPSGSHKVSLSSWYHDRGWAKISN--MTFSNGK-L 206
Qy
                   : | | | | : | :
                                      1 1: 1 :1: :11 :1 111 1
          113 ----MHKGDQEPQIAAHVISEAS----SKTTSVLQW-APKGYYTLSNNLVTLENGKQL 161
Db
          207 IVNQDGFYYLYANICFRHHETSGDLATEYLQLMVYVTKTSIKIP--SSHTLMKGGSTKYW 264
QУ
               1: | | | | : | :
                                      | | ::
                                                  162 AVKRQGFYYIYTQVTFCSNR-----ETLSQAPFIASLCLKSPSGSERILLRAANTH-- 212
Db
QУ
          265 SGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLDPDQDATYFGAFKV 313
                     []::|| |:|:|| : : |::|| :
                                                   213 SSSKPCGQQSIHLGGVFELQSGASVFVNVTDPSQVSHGTGFTSFGLLKL 261
Db
RESULT 12
TNF6 RAT
ID
     TNF6 RAT
                   STANDARD;
                                 PRT;
                                      278 AA.
AC
     P36940;
DT
     01-JUN-1994 (Rel. 29, Created)
     01-JUN-1994 (Rel. 29, Last sequence update)
DT
DT
     28-FEB-2003 (Rel. 41, Last annotation update)
    Tumor necrosis factor ligand superfamily member 6 (FAS antigen
DE
     ligand).
DE
GN
    TNFSF6 OR FASL OR APTILG1.
    Rattus norvegicus (Rat).
OS
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
OC
OX
    NCBI TaxID=10116;
RN
    [1]
    SEQUENCE FROM N.A.
RP
    MEDLINE=94084792; PubMed=7505205;
RX
RA
    Suda T., Takahashi T., Golstein P., Nagata S.;
    "Molecular cloning and expression of the Fas ligand, a novel member
RT
    of the tumor necrosis factor family.";
RT
    Cell 75:1169-1178(1993).
RL
CC
    -!- FUNCTION: Cytokine that binds to TNFRSF6/FAS, a receptor that
CC
        transduces the apoptotic signal into cells. May be involved in
        cytotoxic T cell mediated apoptosis and in T cell development.
CC
        TNFRSF6/FAS-mediated apoptosis may have a role in the induction of
CC
CC
        peripheral tolerance, in the antigen-stimulated suicide of mature
CC
        T cells, or both. Binding to the decoy receptor TNFRSF6B/DcR3
CC
        modulates its effects (By similarity).
CC
    -!- SUBUNIT: Homotrimer (Probable).
    -!- SUBCELLULAR LOCATION: Type II membrane protein and secreted (By
CC
CC
        similarity).
CC
    -!- TISSUE SPECIFICITY: EXPRESSED IN ACTIVATED SPLENOCYTES AND
CC
        THYMOCYTES. MODERATE OR WEAK EXPRESSION FOUND IN SMALL INTESTINES,
CC
        KIDNEY AND LUNG.
CC
    -!- INDUCTION: BY PMA/IONOMYCIN AND CONCAVALIN/INTERLEUKIN-2.
    -!- PTM: The soluble form derives from the membrane form by
```

```
CC
          proteolytic processing (By similarity).
 CC
     -!- SIMILARITY: Belongs to the tumor necrosis factor family.
     CC
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     or send an email to license@isb-sib.ch).
CC
     DR
     EMBL; U03470; AAC52129.1; -.
DR
     PIR; A49266; A49266.
DR
     HSSP; P01375; 4TSV.
DR
     InterPro; IPR008064; Fas ligand.
     InterPro; IPR006053; TNF abc.
DR
     InterPro; IPR006052; TNF family.
DR
     InterPro; IPR008983; TNF like.
DR
     InterPro; IPR003636; TNF subf.
DR
     Pfam; PF00229; TNF; 1.
DR
     PRINTS; PR01681; FASLIGAND.
DR
     PRINTS; PR01234; TNECROSISFCT.
DR
     ProDom; PD002012; TNF subf; 1.
     SMART; SM00207; TNF; 1.
DR
     PROSITE; PS00251; TNF 1; 1.
     PROSITE; PS50049; TNF 2; 1.
KW
     Cytokine; Apoptosis; \overline{\text{T}}ransmembrane; Glycoprotein; Signal-anchor.
FT
     CHAIN
           1 278
                                 TUMOR NECROSIS FACTOR LIGAND SUPERFAMILY
FT
                                 MEMBER 6, MEMBRANE FORM.
FT
     CHAIN 127
                       278
                                  TUMOR NECROSIS FACTOR LIGAND SUPERFAMILY
FT
                                 MEMBER 6, SOLUBLE FORM (BY SIMILARITY).
     DOMAIN 1
FT
                      77
                                 CYTOPLASMIC (POTENTIAL).
     TRANSMEM 78
FT
                       99
                                 SIGNAL-ANCHOR (TYPE-II MEMBRANE PROTEIN)
FT
   DOMAIN 100 278 EXTRACELLULAR (POTENTIAL).

DOMAIN 4 69 PRO-RICH.

DOMAIN 45 58 POLY-PRO.

SITE 126 127 CLEAVAGE (BY SIMILARITY).

DISULFID 199 230 POTENTIAL.

CARBOHYD 116 116 N-LINKED (GLCNAC. . . ) (POTENTIAL).

CARBOHYD 247 247 N-LINKED (GLCNAC. . . ) (POTENTIAL).

CARBOHYD 257 257 N-LINKED (GLCNAC. . . ) (POTENTIAL).

CARBOHYD 257 257 N-LINKED (GLCNAC. . . ) (POTENTIAL).
                                 (POTENTIAL).
FT
FT
FT
FT
FT
FT
FT CARBOHYD
FT CARBOHYD
SO
               278 AA; 31140 MW; 2898E18A862CEAC6 CRC64;
   SEQUENCE
  Query Match
                        10.4%; Score 175.5; DB 1; Length 278;
  Best Local Similarity 20.3%; Pred. No. 8.4e-08;
 Matches 64; Conservative 47; Mismatches 106; Indels 99; Gaps
           21 GPGAPHEGPLHAPPPPAPHQPPAASRSM-----FVALLGLGL 57
Qy
             39 GPGQRRPPP--PPPPPSPLPPPSQPPPLPPLSPLKKKDNIELWLPVIFFMVLVALVGMGL 96
Db
          58 GQVVCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCR 117
Qу
           97 G-----MYQLFHLQKELAELREFTNHSL-RVSSFEKQIANPSTPSETKKPRSV---- 143
Db
Qу
         118 RIKQAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPS 177
```

```
1111
          144 -----AHLTGNPR---- 151
 Db
          178 GSHKVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQ 237
 Qу
               : :: |
          152 -SRSIPL-EWEDTYGTALISGVKYKKGGLVINEAGLYFVYSKVYFRGQSCN----SQPLS 205
 Db
 Qу
          238 LMVYVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPS 297
                206 HKVYM--RNFKYPGDLVLMEEKKLNYCT-TGQIWAHSSYLGAVFNLTVADHLYVNISQLS 262
 Db
          298 LLDPDQDATYFGAFKV 313
 Qу
              1:: :: 1:|| :|:
          263 LINFEESKTFFGLYKL 278
RESULT 13
TNF5 CALJA
     TNF5 CALJA
                  STANDARD;
                                 PRT; 261 AA.
AC
     Q9BDN3;
DT
     28-FEB-2003 (Rel. 41, Created)
DT
     28-FEB-2003 (Rel. 41, Last sequence update)
DT
     28-FEB-2003 (Rel. 41, Last annotation update)
     Tumor necrosis factor ligand superfamily member 5 (CD40 ligand) (CD40-
DE
     L) (CD154 protein).
GN
     TNFSF5 OR CD40LG OR CD40L.
OS
     Callithrix jacchus (Common marmoset).
     Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
OC
     Mammalia; Eutheria; Primates; Platyrrhini; Callitrichidae;
OC
     Callithrix.
OX
     NCBI TaxID=9483;
RN
     [1]
RP
     SEQUENCE FROM N.A.
RC
     TISSUE=Lymphocytes;
RX
     MEDLINE=21383618; PubMed=11491535;
     Villinger F., Bostik P., Mayne A.E., King C.L., Genain C.P.,
RA
     Weiss W.R., Ansari A.A.;
RA
RT
     "Cloning, sequencing, and homology analysis of nonhuman primate
RT
     Fas/Fas-ligand and co-stimulatory molecules.";
RL
     Immunogenetics 53:315-328(2001).
     -!- FUNCTION: Cytokine that binds to TNFRSF5. Mediates B-cell
CC
        proliferation in the absence of co-stimulus as well as IgE
CC
CC
        production in the presence of IL-4. Involved in immunoglobulin
CC
        class switching (By similarity).
CC
    -!- SUBUNIT: Homotrimer (By similarity).
    -!- SUBCELLULAR LOCATION: Type II membrane protein. Also exists as an
CC
        extracellular soluble form (By similarity).
CC
CC
    -!- PTM: The soluble form derives from the membrane form by
        proteolytic processing (By similarity).
CC
    -!- SIMILARITY: Belongs to the tumor necrosis factor family.
CC
CC
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CC
     ________
DR
     EMBL; AF344844; AAK37603.1; -.
DR
    HSSP; P29965; 1ALY.
DR
    GO; GO:0016021; C:integral to membrane; ISS.
DR
    GO; GO:0005174; F:CD40 receptor binding; ISS.
DR
    GO; GO:0042100; P:B-cell proliferation; ISS.
    GO; GO:0006954; P:inflammatory response; ISS.
DR
    GO; GO:0007159; P:leukocyte cell adhesion; ISS.
DR
DR
    GO; GO:0030168; P:platelet activation; ISS.
DR
    InterPro; IPR003263; TNF 5.
DR
    InterPro; IPR006052; TNF family.
DR
    InterPro; IPR008983; TNF like.
DR
    InterPro; IPR003636; TNF subf.
    Pfam; PF00229; TNF; 1.
DR
DR
    PRINTS; PR01702; CD40LIGAND.
    ProDom; PD008600; TNF_5; 1.
DR
    ProDom; PD002012; TNF subf; 1.
DR
    SMART; SM00207; TNF; 1.
DR
DR
    PROSITE; PS00251; TNF 1; 1.
DR
    PROSITE; PS50049; TNF 2; 1.
    Cytokine; Transmembrane; Glycoprotein; Signal-anchor.
KW
FT
    CHAIN
                1
                   261
                             TUMOR NECROSIS FACTOR LIGAND SUPERFAMILY
FT
                             MEMBER 5, MEMBRANE FORM.
FT
    CHAIN 113
                    261
                             TUMOR NECROSIS FACTOR LIGAND SUPERFAMILY
FT
                             MEMBER 5, SOLUBLE FORM (BY SIMILARITY).
    TRANSMEM 23
FT
                    22
                            CYTOPLASMIC (POTENTIAL).
FT
                     43
                             SIGNAL-ANCHOR (TYPE-II MEMBRANE PROTEIN)
FT
                             (POTENTIAL).
FT
              44 261
    DOMAIN
                             EXTRACELLULAR (POTENTIAL).
                  11.
218
240
29360
FT
             112
    SITE
                             CLEAVAGE (BY SIMILARITY).
FT
    DISULFID
              178
                            POTENTIAL.
FΤ
    CARBOHYD
              240
                            N-LINKED (GLCNAC. . .) (POTENTIAL).
    SEQUENCE 261 AA; 29360 MW; 10CA588D923754EB CRC64;
SQ
 Query Match
                      10.1%; Score 169.5; DB 1; Length 261;
 Best Local Similarity 24.6%; Pred. No. 2.5e-07;
         71; Conservative 55; Mismatches 120; Indels 43; Gaps
                                                                 15:
Qу
         33 PPPPAPHQPPAASRSMFVALLGLGL-GQVVCSVALFFYFRAQMDPNRISEDGTHCIYRIL 91
            Db
          8 PVPRSAATGPPVSMKIFMYLLTVFLITQMIGSALFAVYLHRRLD--KIEDE-----R 57
Qу
         92 RLHENADFQDT--TLESQDTKLIPDSCRRIKQAFQGAVQKELQHIVGSQHIRAEKAMVDG 149
             58 NLHEDFVFMKTIQRCNTGERSLSLLNCEEIKSQFEGFV-KDIM-----LNKEEKKKEN 109
Db
Qу
        150 SWLDLAKRSKLEAQPFAHLTINATDIPSGSHKVSLSSWYHDRGWAKISN--MTFSNGK-L 206
            Db
        110 SF-EMQKGDQ-NPQIAAHVISEAS----SKTTSVLQW-AEKGYYTMSNNLVTLENGKQL 161
QУ
        207 IVNQDGFYYLYANICFRHHETSGDLATEYLQLMVYVTKTSIKIPS--SHTLMKGGSTKYW 264
             Db
        162 TVKRQGLYYIYAQVTFCSNREASSQAP-----FIASLCLKPPNRFERILLRAANTH-- 212
        265 SGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLDPDQDATYFGAFKV 313
Qу
```

```
RESULT 14
 TNF5 AOTTR
 ID
     TNF5 AOTTR
                   STANDARD;
                                  PRT; 261 AA.
 AC
     Q9BDM3;
 DT
     28-FEB-2003 (Rel. 41, Created)
 DT
     28-FEB-2003 (Rel. 41, Last sequence update)
     28-FEB-2003 (Rel. 41, Last annotation update)
DΕ
     Tumor necrosis factor ligand superfamily member 5 (CD40 ligand) (CD40-
     L) (CD154 protein).
DE
     TNFSF5 OR CD40LG OR CD40L.
GN
     Aotus trivirgatus (Night monkey) (Douroucouli).
OS
     Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
     Mammalia; Eutheria; Primates; Platyrrhini; Cebidae; Aotinae; Aotus.
OC
OX
     NCBI TaxID=9505;
RN
     [1]
RP
     SEQUENCE FROM N.A.
RC
     TISSUE=Lymphocytes;
RX
     MEDLINE=21383618; PubMed=11491535;
RA
     Villinger F., Bostik P., Mayne A.E., King C.L., Genain C.P.,
RA
     Weiss W.R., Ansari A.A.;
RT
     "Cloning, sequencing, and homology analysis of nonhuman primate
RT
     Fas/Fas-ligand and co-stimulatory molecules.";
RL
     Immunogenetics 53:315-328(2001).
     -!- FUNCTION: Cytokine that binds to TNFRSF5. Mediates B-cell
CC
CC
         proliferation in the absence of co-stimulus as well as IgE
CC
         production in the presence of IL-4. Involved in immunoglobulin
CC
         class switching (By similarity).
CC
     -!- SUBUNIT: Homotrimer (By similarity).
     -!- SUBCELLULAR LOCATION: Type II membrane protein. Also exists as an
CC
CC
         extracellular soluble form (By similarity).
     -!- PTM: The soluble form derives from the membrane form by
CC
CC
        proteolytic processing (By similarity).
     -!- SIMILARITY: Belongs to the tumor necrosis factor family.
CC
     CC
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CC
     between the Swiss Institute of Bioinformatics and the EMBL outstation -
     the European Bioinformatics Institute. There are no restrictions on its
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     use by non-profit institutions as long as its content is in no way
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    entities requires a license agreement (See http://www.isb-sib.ch/announce/
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     or send an email to license@isb-sib.ch).
CC
    ______
DR
    EMBL; AF344860; AAK37542.1; -.
DR
    HSSP; P29965; 1ALY.
    GO; GO:0016021; C:integral to membrane; ISS.
DR
    GO; GO:0005174; F:CD40 receptor binding; ISS.
DR
    GO; GO:0042100; P:B-cell proliferation; ISS.
DR
    GO; GO:0006954; P:inflammatory response; ISS.
DR
DR
    GO; GO:0007159; P:leukocyte cell adhesion; ISS.
    GO; GO:0030168; P:platelet activation; ISS.
DR
    InterPro; IPR003263; TNF 5.
DR
    InterPro; IPR006052; TNF_family.
DR
DR
    InterPro; IPR008983; TNF like.
DR
    InterPro; IPR003636; TNF subf.
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Pfam; PF00229; TNF; 1.
 DR
 DR
     PRINTS; PR01702; CD40LIGAND.
 DR
     ProDom; PD008600; TNF 5; 1.
     ProDom; PD002012; TNF subf; 1.
 DR
     SMART; SM00207; TNF; 1.
 DR
     PROSITE; PS00251; TNF 1; 1.
 DR
     PROSITE; PS50049; TNF 2; 1.
 KW
     Cytokine; Transmembrane; Glycoprotein; Signal-anchor.
FT
     CHAIN
                      261
                               TUMOR NECROSIS FACTOR LIGAND SUPERFAMILY
FT
                               MEMBER 5, MEMBRANE FORM.
FT
     CHAIN 113 261
                               TUMOR NECROSIS FACTOR LIGAND SUPERFAMILY
FT
                               MEMBER 5, SOLUBLE FORM (BY SIMILARITY).
     DOMAIN 1 22
TRANSMEM 23 43
FT
                           CYTOPLASMIC (POTENTIAL).
FT
                             SIGNAL-ANCHOR (TYPE-II MEMBRANE PROTEIN)
FΤ
                              (POTENTIAL).
    DOMAIN 44 261 EXTRACELLULAR (POTENTIAL).

SITE 112 113 CLEAVAGE (BY SIMILARITY).

DISULFID 178 218 POTENTIAL.

CARBOHYD 240 240 N-LINKED (GLCNAC. . .) (POTENTIAL).
FT
FT
FT
FT
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             Db
           6 HQPAPRSAATGLPVSMKIFMYLLTVFLITQMIGSALFAVYLHRRLD--KIEDE----- 56
          90 ILRLHENADFQDT--TLESQDTKLIPDSCRRIKQAFQGAVQKELQHIVGSQHIRAEKAMV 147
QУ
               57 -RNLHEDFVFMKTIQRCNTGERSLSLLNCEEIKSQFEGFV-KDIM-----LNKEEKKK 107
Db
         148 DGSWLDLAKRSKLEAQPFAHLTINATDIPSGSHKVSLSSWYHDRGWAKISN--MTFSNGK 205
Qу
             108 ENSF-EMQKGDQ-NPQIAAHVISEAS----SKTTSVLQW-AEKGYYTMSNNLVTLENGK 159
Db
         206 -LIVNQDGFYYLYANICFRHHETSGDLATEYLQLMVYVTKTSIKIPS--SHTLMKGGSTK 262
QУ
             160 QLTVKRQGLYYIYAQVTFCSNREASSQAP-----FIASLCLKPPNRFERILLRAANTH 212
Db
         263 YWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLDPDQDATYFGAFKV 313
Qу
             Db
         213 --SSAKPCGQQSIHLGGIFELQPGASVFVNVTDPSQVSHGTGFTSFGLLKL 261
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TNF5 HUMAN
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   P29965;
    01-APR-1993 (Rel. 25, Created)
DT 01-APR-1993 (Rel. 25, Last sequence update)
   15-MAR-2004 (Rel. 43, Last annotation update)
    Tumor necrosis factor ligand superfamily member 5 (CD40 ligand) (CD40-
    L) (TNF-related activation protein) (TRAP) (T cell antigen Gp39)
DE
    (CD154 antigen).
DE
GN
    TNFSF5 OR CD40LG OR CD40L OR TRAP.
```

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OS
      Homo sapiens (Human).
 OC
      Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC
      Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
 OX
      NCBI TaxID=9606;
 RN
      [1]
 RP
      SEQUENCE FROM N.A.
 RX
      MEDLINE=93076854; PubMed=1280226;
 RA
      Graf D., Korthaeuer U., Mages H.W., Senger G., Kroczek R.A.;
 RT
      "Cloning of TRAP, a ligand for CD40 on human T cells.";
      Eur. J. Immunol. 22:3191-3194(1992).
 RL
 RN
      [2]
 RΡ
      SEQUENCE FROM N.A.
 RX
      MEDLINE=93049181; PubMed=1385114;
      Hollenbaugh D., Grosmaire L.S., Kullas C.D., Chalupny J.N.,
 RA
      Braesch-Andersen S., Noelle R.J., Stamenkovic I., Ledbetter J.A.,
 RA
 RA
      "The human T cell antigen gp39, a member of the TNF gene family, is a
 RT
      ligand for the CD40 receptor: expression of a soluble form of gp39
 RT
 RT
      with B cell co-stimulatory activity.";
      EMBO J. 11:4313-4321(1992).
RL
RN
      [3]
RP
     SEQUENCE FROM N.A., AND VARIANTS HIGHL 128-ARG-GLY-129 AND PRO-235.
RX
     MEDLINE=93145330; PubMed=7678782;
     Aruffo A., Farrington M., Hollenbaugh D., Li X., Milatovich A.,
RA
     Nonoyama S., Bajorath J., Grosmaire L.S., Stenkamp R., Neubauer M.,
     Roberts R.L., Noelle R.J., Ledbetter J.A., Francke U., Ochs H.D.;
RA
RT
     "The CD40 ligand, gp39, is defective in activated T cells from
     patients with X-linked hyper-IgM syndrome.";
RT
     Cell 72:291-300(1993).
RL
RN
     [4]
RΡ
     SEQUENCE FROM N.A.
     MEDLINE=93094757; PubMed=1281209;
RX
     Spriggs M.K., Armitage R.J., Strockbine L., Clifford K.N.,
RA
RA
     Macduff B.M., Sato T.A., Maliszewski C.R., Fanslow W.C.;
     "Recombinant human CD40 ligand stimulates B cell proliferation and
RТ
RT
     immunoglobulin E secretion.";
RL
     J. Exp. Med. 176:1543-1550(1992).
RN
RP
     SEQUENCE FROM N.A.
RX
     MEDLINE=93138085; PubMed=7678552;
     Gauchat J.F.M., Aubry J.-P., Mazzei G.J., Life P., Jomotte T.,
RA
     Elson G., Bonnefoy J.Y.;
     "Human CD40-ligand: molecular cloning, cellular distribution and
RT
RТ
     regulation of expression by factors controlling IgE production.";
     FEBS Lett. 315:259-266(1993).
RL
RN
RΡ
     SEQUENCE FROM N.A.
     Shimadzu M., Terasaki H., Ninomiya R., Shimizu S., Nunoi H.,
RA
RA
     Matsuda I.;
     Submitted (FEB-1995) to the EMBL/GenBank/DDBJ databases.
RL
RN
     SEQUENCE OF 113-117, AND PROCESSING.
RP
RX
     MEDLINE=96198042; PubMed=8626375;
     Pietravalle F., Lecoanet-Henchoz S., Blasey H., Aubry J.-P., Elson G.,
RA
RA
     Edgerton M.D., Bonnefoy J.-Y., Gauchat J.-F.;
     "Human native soluble CD40L is a biologically active trimer, processed
RT
RT
     inside microsomes.";
```

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RL
      J. Biol. Chem. 271:5965-5967(1996).
 RN
 RP
      X-RAY CRYSTALLOGRAPHY (2.0 ANGSTROMS) OF 116-261.
 RX
      MEDLINE=96131874; PubMed=8589998;
      Karpsusas M., Hsu Y.-M., Wang J.-H., Thompson J., Lederman S.,
 RA
 RA
      Chess L., Thomas D.;
 RT
      "2-A crystal structure of an extracellular fragment of human CD40
RT
      ligand.";
RL
      Structure 3:1031-1039(1995).
RN
RP
      3D-STRUCTURE MODELING OF COMPLEX WITH CD40.
RX
     MEDLINE=98266353; PubMed=9605317;
      Singh J., Garber E., van Vlijmen H., Karpsusas M., Hsu Y.-M.,
RA
      Zheng Z., Naismith J.H., Thomas D.;
RA
     "The role of polar interactions in the molecular recognition of {\tt CD40L}
RT
RT
     with its receptor CD40.";
RL
     Protein Sci. 7:1124-1135(1998).
RN
     [10]
RP
     VARIANTS HIGM1 ARG-36 AND GLY-140.
RX
     MEDLINE=93156839; PubMed=7679206;
RA
     Korthaeuer U., Graf D., Mages H.W., Briere F., Padayachee M.,
     Malcolm S., Ugazio A.G., Notarangelo L.D., Levinsky R.J.,
RA
RA
     Kroczek R.A.;
RT
     "Defective expression of T-cell CD40 ligand causes X-linked
RT
     immunodeficiency with hyper-IqM.";
     Nature 361:539-541(1993).
RL
RN
     [11]
RP
     VARIANT HIGM1 GLU-123.
RX
     MEDLINE=93156840; PubMed=8094231;
     Disanto J.P., Bonnefoy J.Y., Gauchat J.F.M., Fischer A.,
RA
RA
     de Saint Basile G.;
     "CD40 ligand mutations in X-linked immunodeficiency with hyper-IgM.";
RT
RL
     Nature 361:541-543(1993).
RN
RP
     VARIANTS HIGM1 PRO-155; ASP-211 AND VAL-227.
RX
     MEDLINE=93174270; PubMed=7679801;
RA
     Allen R.C., Armitage R.J., Conley M.E., Rosenblatt H., Jenkins N.A.,
RA
     Copeland N.G., Bedell M.A., Edelhoff S., Disteche C.M.,
RA
     Simoneaux D.K., Fanslow W.C., Belmont J.W., Spriggs M.K.;
     "CD40 ligand gene defects responsible for X-linked hyper-IgM
RT
RT
     syndrome.";
RL
     Science 259:990-993(1993).
RN
     [13]
RP
     VARIANTS HIGM1 ALA-126; ARG-140 AND GLU-144.
RX
     MEDLINE=95233438; PubMed=7717401;
     Macchi P., Villa A., Strina D., Sacco M.G., Morali F., Brugnoni D.,
RA
     Giliani S., Mantuano E., Fasth A., Andersson B., Zegers B.J.M.,
RA
     Cavagni G., Reznick I., Levy J., Zan-Bar I., Porat Y., Airo P.,
RA
RA
     Plebani A., Vezzoni P., Notarangelo L.D.;
     "Characterization of nine novel mutations in the CD40 ligand gene in
RΤ
RT
     patients with X-linked hyper IgM syndrome of various ancestry.";
    Am. J. Hum. Genet. 56:898-906(1995).
RN
     VARIANTS HIGM1 PRO-155 AND VAL-227, AND VARIANT ARG-219.
RP
RX
    MEDLINE=96133533; PubMed=8550833;
RA
    Lin Q., Rohrer J., Allen R.C., Larche M., Greene J.M., Shigeoka A.O.,
RA
    Gatti R.A., Derauf D.C., Belmont J.W., Conley M.E.;
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RT
     "A single strand conformation polymorphism study of CD40 ligand.
RT
     Efficient mutation analysis and carrier detection for X-linked hyper
RT
     IgM syndrome.";
RL
     J. Clin. Invest. 97:196-201(1996).
RN
     [15]
RP
     VARIANTS HIGM1 ARG-36; CYS-140; SER-231; MET-254 AND GLY-227 DEL.
RX
     MEDLINE=97295077; PubMed=9150729;
RA
     Nonoyama S., Shimadzu M., Toru H., Seyama K., Nunoi H., Neubauer M.,
RA
     Yata J.-I., Och H.D.;
     "Mutations of the CD40 ligand gene in 13 Japanese patients with
RT
RT
     X-linked hyper-IgM syndrome.";
RL
     Hum. Genet. 99:624-627(1997).
     -!- FUNCTION: Mediates B-cell proliferation in the absence of co-
CC
CC
         stimulus as well as IgE production in the presence of IL-4.
CC
         Involved in immunoglobulin class switching.
CC
     -!- SUBUNIT: Homotrimer.
     -!- SUBCELLULAR LOCATION: Type II membrane protein. Also exists as an
CC
CC
        extracellular soluble form.
     -!- TISSUE SPECIFICITY: Specifically expressed on activated CD4+
CC
CC
        T-lymphocytes.
CC
     -!- PTM: The soluble form derives from the membrane form by
CC
        proteolytic processing.
CC
     -!- DISEASE: Defects in TNFSF5 are the cause of X-linked
CC
        immunodeficiency with hyper-IgM type 1 (HIGM1) [MIM:308230]. HIGM1
CC
        is an immunoglobulin isotype switch defect characterized by
CC
        elevated concentrations of serum IgM and decreased amounts of all
CC
        other isotypes. Affected males present at an early age (usually
CC
        within the first year of life) recurrent bacterial and
CC
        opportunistic infections, including pneumocystis carinii pneumonia
CC
        and intractable diarrhea due to cryptosporidium infection. Despite
CC
        substitution treatment with intravenous immunoglobulin, the
CC
        overall prognosis is rather poor, with a death rate of about 10\%
CC
        before adolescence.
CC
    -!- SIMILARITY: Belongs to the tumor necrosis factor family.
CC
    -!- DATABASE: NAME=CD40Lbase;
        NOTE=European CD40L defect database (mutation db);
CC
CC
        WWW="http://www.expasy.org/cd40lbase/";
CC
        FTP="ftp://ftp.expasy.org/databases/cd40lbase".
    -!- DATABASE: NAME=PROW; NOTE=CD quide CD154 entry;
CC
        WWW="http://www.ncbi.nlm.nih.gov/prow/cd/cd154.htm".
CC
    CC
CC
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    or send an email to license@isb-sib.ch).
CC
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DR
    EMBL; Z15017; CAA78737.1; -.
DR
DR
    EMBL; X67878; CAA48077.1; -.
DR
    EMBL; L07414; AAA35662.1; -.
    EMBL; D31797; BAA06599.1; -.
    EMBL; D31793; BAA06599.1; JOINED.
DR
    EMBL; D31794; BAA06599.1; JOINED.
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DR

DR

EMBL; D31795; BAA06599.1; JOINED.

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EMBL; D31796; BAA06599.1; JOINED.
DR
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DR
     PDB; 1ALY; 17-SEP-97.
DR
     PDB; 119R; 22-MAY-02.
DR
     Genew; HGNC:11935; TNFSF5.
DR
     MIM; 300386; -.
     MIM; 308230; -.
DR
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DR
     GO; GO:0005625; C:soluble fraction; TAS.
DR
DR
     GO; GO:0005174; F:CD40 receptor binding; IPI.
DR
     GO; GO:0006916; P:anti-apoptosis; IDA.
DR
     GO; GO:0042100; P:B-cell proliferation; IDA.
DR
     GO; GO:0006954; P:inflammatory response; IDA.
     GO; GO:0045190; P:isotype switching; ISS.
DR
     GO; GO:0007159; P:leukocyte cell adhesion; NAS.
DR
DR
     GO; GO:0030168; P:platelet activation; IDA.
DR
     GO; GO:0007165; P:signal transduction; ISS.
DR
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DR
    InterPro; IPR006052; TNF family.
    InterPro; IPR008983; TNF like.
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Qу
            1 :1: 11 : 1 1:: 1 | :: | :: | ::
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Db
Qу
         103 -TLESQDTKLIPDSCRRIKQAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLE 161
                70 QRCNTGERSLSLLNCEEIKSQFEGFV-KDIM-----LNKEETKKENSF-EMQKGDQ-N 119
Db
        162 AQPFAHLTINATDIPSGSHKVSLSSWYHDRGWAKISN--MTFSNGK-LIVNQDGFYYLYA 218
Qу
             120 PQIAAHVISEAS----SKTTSVLQW-AEKGYYTMSNNLVTLENGKQLTVKRQGLYYIYA 173
Db
        219 NICFRHHETSGDLATEYLQLMVYVTKTSIKIPS--SHTLMKGGSTKYWSGNSEFHFYSIN 276
Qу
             : | : : | :: :| | :: :| |
        174 QVTFCSNREASSQAP-----FIASLCLKSPGRFERILLRAANTH--SSAKPCGQQSIH 224
Db
        277 VGGFFKLRSGEEISIEVSNPSLLDPDQDATYFGAFKV 313
Qy
            225 LGGVFELQPGASVFVNVTDPSQVSHGTGFTSFGLLKL 261
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